

=&gt; d his 1

(FILE 'MEDLINE, BIOSIS, EMBASE, SCISEARCH, HCAPLUS' ENTERED AT 16:12:08  
ON 21 FEB 2003)

L35 87 DUP REM L34 L22 (50 DUPLICATES REMOVED)

=&gt; d que 135

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L1      28 SEA FILE=REGISTRY SKITHRIHWESASLL/SQSP
L2      19 SEA FILE=HCAPLUS L1
L3      118 SEA FILE=HCAPLUS JACKOWSKI G?/AU
L4      47 SEA FILE=HCAPLUS THATCHER B?/AU
L5      2949 SEA FILE=HCAPLUS MARSHALL J?/AU
L6      30 SEA FILE=HCAPLUS VREES T?/AU
L7      30 SEA FILE=HCAPLUS YANTHA J?/AU
L8      3051 SEA FILE=HCAPLUS (L3 OR L4 OR L5 OR L6 OR L7)
L9      6723 SEA FILE=HCAPLUS COMPLEMENT(3A)C3?
L10     13 SEA FILE=HCAPLUS L8 AND L9
L11     7 SEA FILE=HCAPLUS L2 AND L8
L12     13 SEA FILE=HCAPLUS L10 OR L11
L13     13846 SEA L8
L14     27120 SEA L9
L15     0 SEA L13 AND L14
L16     9 SEA FILE=HCAPLUS L2 AND (CARDIO? OR CARDIA? OR HEART?)
L17     13 SEA FILE=HCAPLUS L9 AND ((DETECT? OR MEASUR? OR ASSAY? OR
      DIAGNOS?) (5A) (CARDIO? OR CARDIA? OR HEART?))
L18     8 SEA FILE=HCAPLUS L2 AND (MASS(3A)SPECTRO?)
L19     31 SEA FILE=HCAPLUS L9 AND (MASS(3A)SPECTRO?)
L20     7 SEA FILE=HCAPLUS L2 AND (LASER(3A)DESORPT?)
L21     18 SEA FILE=HCAPLUS L9 AND (LASER(3A)DESORPT?)
L22     45 SEA FILE=HCAPLUS L12 OR (L16 OR L17 OR L18 OR L19 OR L20 OR
      L21)
L23     70 SEA L14 AND ((DETECT? OR MEASUR? OR ASSAY? OR DIAGNOS?) (5A) (CAR
      DIO? OR CARDIA? OR HEART?))
L24     59 SEA L14 AND (MASS(3A) SPECTRO?)
L25     21 SEA L14 AND (LASER(3A) DESORPT?)
L26     129 SEA L15 OR (L23 OR L24 OR L25)
L29     25 SEA L26 AND C3B
L32     104 SEA L26 NOT L29
L34     92 SEA L32 AND (DETECT? OR MEASUR? OR ASSAY? OR DIAGNOS?)
L35     87 DUP REM L34 L22 (50 DUPLICATES REMOVED)

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=&gt; d ibib abs 135 1-87

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L35 ANSWER 1 OF 87 HCAPLUS COPYRIGHT 2003 ACS          DUPLICATE 1
ACCESSION NUMBER:      2002:977609 HCAPLUS
DOCUMENT NUMBER:       138:50922
TITLE:                 Human cDNA sequences and their encoded proteins and
                        diagnostic and therapeutic uses
INVENTOR(S):           Anderson, David W.; Guo, Xiaojia; Gusev, Vladimir Y.;
                        Herrmann, John L.; Li, Li; Mezes, Peter S.; Pena,
                        Carol E. A.; Spaderna, Steven K.; Zhong, Mei
PATENT ASSIGNEE(S):    Curagen Corporation, USA
SOURCE:                PCT Int. Appl., 378 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:          Patent
LANGUAGE:              English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE       |
|--|------|----------|-----------------|------------|
| WO 2002102321  | A2   | 20021227 | WO 2002-US19522 | 20020618   |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,<br>CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,<br>GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,<br>LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,<br>PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,<br>UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,<br>TJ, TM<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,<br>CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,<br>BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |            |
| PRIORITY APPLN. INFO.:   |      |          | US 2001-298994P | P 20010618 |
|  |      |          | US 2001-299134P | P 20010618 |
|  |      |          | US 2001-972446  | A 20011004 |
| AB Disclosed herein are 22 cDNA sequences that encode novel human polypeptides that are members of the following protein families: interleukin-1 receptor/Toll, GNC2 EIF2.alpha. kinase, <b>complement C3</b> , Wnt8, .beta.-thymosin, trypsin, kallikrein, acetyl LDL receptor, neurolysin, cyclic nucleotide-gated olfactory receptor, chloride channel, fatty acid-binding protein, insulin-like growth factor, cytokeratin-18, metalloproteinase, mast cell protease-6, sulfate transporter, cytochrome, chemokine receptor, and carboxypeptidase. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivs., variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, <b>diagnostic</b> and research methods for <b>diagnosis</b> , treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins. |      |          |                 |            |
| L35 ANSWER 2 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 2  |      |          |                 |            |
| ACCESSION NUMBER: 2002:849922 HCAPLUS  |      |          |                 |            |
| DOCUMENT NUMBER: 137:348843  |      |          |                 |            |
| TITLE: Biopolymer marker indicative of disease state having a molecular weight of 2056 daltons   |      |          |                 |            |
| INVENTOR(S): <b>Jackowski, George; Thatcher, Brad; Marshall, John; Yantha, Jason; Vrees, Tammy</b>   |      |          |                 |            |
| PATENT ASSIGNEE(S): Syn.X Pharma, Inc., Can.   |      |          |                 |            |
| SOURCE: PCT Int. Appl., 27 pp.   |      |          |                 |            |
| CODEN: PIXXD2  |      |          |                 |            |
| DOCUMENT TYPE: Patent  |      |          |                 |            |
| LANGUAGE: English  |      |          |                 |            |
| FAMILY ACC. NUM. COUNT: 1  |      |          |                 |            |
| PATENT INFORMATION:  |      |          |                 |            |

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2002088717   | A2   | 20021107 | WO 2002-CA578   | 20020425 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,<br>CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,<br>GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,<br>LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,<br>PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,<br>UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, |      |          |                 |          |

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-845736 A 20010430

AB The instant invention involves the use of a combination of preparatory steps in conjunction with **mass spectroscopy** and time-of-flight **detection** procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with ref. to their ability to evidence at least one particular disease state; thereby enabling a **diagnostician** to gain the ability to characterize either the presence or absence of said at least one disease state relative to recognition of the presence and/or the absence of said biopolymer.

L35 ANSWER 3 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 3

ACCESSION NUMBER: 2002:429206 HCAPLUS

DOCUMENT NUMBER: 137:15797

TITLE: **Diagnostic** and therapeutic compositions and methods related to the human anaphylatoxin C3a receptor

INVENTOR(S): Brown, Joseph P.; Burmer, Glenna C.; Roush, Christine L.; Morningstar, Douglas A.

PATENT ASSIGNEE(S): Lifespan Biosciences, Inc., USA

SOURCE: PCT Int. Appl., 112 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO. | DATE       |
|------------------------|--|----------|-----------------|------------|
| WO 2002044737          | A2   | 20020606 | WO 2001-US45220 | 20011129   |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |            |
| RW:                    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |            |
| AU 2002039417          | A5   | 20020611 | AU 2002-39417   | 20011129   |
| PRIORITY APPLN. INFO.: |  |          | US 2000-250251P | P 20001129 |
|                        |  |          | US 2000-250425P | P 20001130 |
|                        |  |          | US 2000-250452P | P 20001130 |
|                        |  |          | US 2001-330036P | P 20011017 |
|                        |  |          | WO 2001-US45220 | W 20011129 |

AB **Diagnostics**, therapeutics and the like based on anaphylatoxin C3a receptor directed against Alzheimer's disease and Parkinson's disease. The compns. and methods and the like can include one or more of peptide, protein, antibody, and nucleic acid components, and can be useful, for example, as agonists, antagonists, probes, antisense and gene therapy compns. and otherwise as may be desired. Thus, appropriate antigenic peptide portions of the anaphylatoxin C3a receptor are identified which induce antibodies specific for the receptor. The antibodies are purified by immunosorbent chromatog. and protocols provided for their use in immunohistochem. **detection** of the receptor among various tissues of healthy patients and patients with Alzheimer's disease or Parkinson's disease. Altered expression levels are demonstrated between normal

neurons and senile plaques (Alzheimer's disease) and between pigmented or nonpigmented neurons (Parkinson's disease).

L35 ANSWER 4 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 4  
 ACCESSION NUMBER: 2002:833555 HCAPLUS  
 DOCUMENT NUMBER: 137:334915  
 TITLE: Apolipoprotein CIII biopolymer marker indicative of Type II diabetes having a molecular weight of 1097 daltons  
 INVENTOR(S): Jackowski, George; Thatcher, Brad; Marshall, John; Yantha, Jason; Vrees, Tammy  
 PATENT ASSIGNEE(S): Can.  
 SOURCE: U.S. Pat. Appl. Publ., 10 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2002161187 | A1   | 20021031 | US 2001-846352  | 20010430 |
| WO 2002088743 | A2   | 20021107 | WO 2002-CA618   | 20020429 |
| WO 2002088743 | A3   | 20030103 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-846352 A 20010430

AB The instant invention involves the use of a combination of preparatory steps in conjunction with **mass spectroscopy** and time-of-flight **detection** procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with ref. to their ability to evidence at least one particular disease state; thereby enabling a **diagnostician** to gain the ability to characterize either the presence or absence of said at least one disease state relative to recognition of the presence and/or the absence of said biopolymer. Serum samples were analyzed by SELDI-TOF using the Ciphergen PROTEINCHIP system and the disease specific marker identified by the sequence PEVRPTSAVAA and characterized as a apolipoprotein CIII having a mol. wt. of 1097 daltons was found. This marker is indicative of Type II diabetes.

L35 ANSWER 5 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 5  
 ACCESSION NUMBER: 2002:833554 HCAPLUS  
 DOCUMENT NUMBER: 137:334914  
 TITLE: **Complement C3f** biopolymer marker indicative of myocardial infarction and congestive heart failure having a molecular weight of 1449 daltons  
 INVENTOR(S): Jackowski, George; Thatcher, Brad; Marshall, John; Yantha, Jason; Vrees, Tammy

PATENT ASSIGNEE(S): Can.  
SOURCE: U.S. Pat. Appl. Publ., 10 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2002161186 | A1   | 20021031 | US 2001-846349  | 20010430 |
| WO 2002088726 | A2   | 20021107 | WO 2002-CA615   | 20020426 |
| WO 2002088726 | A3   | 20021227 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-846349 A 20010430

AB The instant invention involves the use of a combination of preparatory steps in conjunction with **mass spectroscopy** and time-of-flight **detection** procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with ref. to their ability to evidence at least one particular disease state; thereby enabling a **diagnostician** to gain the ability to characterize either the presence or absence of said at least one disease state relative to recognition of the presence and/or the absence of said biopolymer. Serum samples were analyzed by SELDI-TOF using the Ciphergen PROTEINCHIP system and the disease specific marker identified by the sequence THRIHWESASLL and characterized as a **complement C3f** fragment having a mol. wt. of 1449 daltons was found. This marker is indicative of myocardial infarction, intracerebral hemorrhage, or congestive heart failure.

L35 ANSWER 6 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 6

ACCESSION NUMBER: 2002:833552 HCAPLUS

DOCUMENT NUMBER: 137:334912

TITLE: **Complement C3f** biopolymer marker  
indicative of myocardial infarction and congestive  
heart failure having a molecular weight of 1348  
daltons

INVENTOR(S): **Jackowski, George; Thatcher, Brad;**  
**Marshall, John; Yantha, Jason;**  
**Vrees, Tammy**

PATENT ASSIGNEE(S): Can.  
SOURCE: U.S. Pat. Appl. Publ., 11 pp.  
CODEN: USXXCO

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

US 2002161184 A1 20021031 US 2001-845715 20010430  
 WO 2002088720 A2 20021107 WO 2002-CA608 20020426

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-845715 A 20010430

AB The instant invention involves the use of a combination of preparatory steps in conjunction with **mass spectroscopy** and time-of-flight **detection** procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with ref. to their ability to evidence at least one particular disease state; thereby enabling a **diagnostician** to gain the ability to characterize either the presence or absence of said at least one disease state relative to recognition of the presence and/or the absence of said biopolymer. Serum samples were analyzed by SELDI-TOF using the Ciphergen PROTEINCHIP system and the disease specific marker identified by the sequence HRIHWESASLL and characterized as a **complement C3f** fragment having a mol. wt. of 1348 daltons was found. This marker is indicative of myocardial infarction, intracerebral hemorrhage, or congestive heart failure.

L35 ANSWER 7 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 7

ACCESSION NUMBER: 2002:833550 HCAPLUS

DOCUMENT NUMBER: 137:334910

TITLE: **Complement C3f** biopolymer marker  
 indicative of myocardial infarction and congestive heart failure having a molecular weight of 1865 daltons

INVENTOR(S): **Jackowski, George; Thatcher, Brad;**  
**Marshall, John; Yantha, Jason;**  
**Vrees, Tammy**

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 10 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2002161182 | A1   | 20021031 | US 2001-846345  | 20010430 |
| WO 2002088174 | A2   | 20021107 | WO 2002-CA622   | 20020429 |
| WO 2002088174 | A3   | 20030116 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 PRIORITY APPLN. INFO.: US 2001-846345 A 20010430

AB The instant invention involves the use of a combination of preparatory steps in conjunction with **mass spectroscopy** and time-of-flight **detection** procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with ref. to their ability to evidence at least one particular disease state; thereby enabling a **diagnostician** to gain the ability to characterize either the presence or absence of said at least one disease state relative to recognition of the presence and/or the absence of said biopolymer. Serum samples were analyzed by SELDI-TOF using the Ciphergen PROTEINCHIP system and the disease specific marker identified by the sequence SSKITHRIHWESASLL and characterized as a **complement C3f** fragment having a mol. wt. of 1865 daltons was found. This marker is indicative of myocardial infarction, intracerebral hemorrhage, Type II diabetes, or congestive heart failure.

L35 ANSWER 8 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 8  
 ACCESSION NUMBER: 2002:833549 HCAPLUS  
 DOCUMENT NUMBER: 137:334909  
 TITLE: **Complement C3f** biopolymer marker  
 indicative of myocardial infarction and congestive  
 heart failure having a molecular weight of 2021  
 daltons  
 INVENTOR(S): **Jackowski, George; Thatcher, Brad;**  
**Marshall, John; Yantha, Jason;**  
**Vrees, Tammy**  
 PATENT ASSIGNEE(S): Can.  
 SOURCE: U.S. Pat. Appl. Publ., 10 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2002161181 | A1   | 20021031 | US 2001-846344  | 20010430 |
| WO 2002088711 | A2   | 20021107 | WO 2002-CA627   | 20020429 |
| WO 2002088711 | A3   | 20030116 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-846344 A 20010430

AB The instant invention involves the use of a combination of preparatory steps in conjunction with **mass spectroscopy** and time-of-flight **detection** procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with ref. to their ability to evidence at least one particular disease state; thereby enabling a **diagnostician** to gain the ability to characterize either the presence or absence of said at least one disease state relative

to recognition of the presence and/or the absence of said biopolymer. Serum samples were analyzed by SELDI-TOF using the Ciphergen PROTEINCHIP system and the disease specific marker identified by the sequence SSKITHRIHWESASLLR and characterized as a **complement C3f** fragment having a mol. wt. of 2021 daltons was found. This marker is indicative of myocardial infarction, Type II diabetes, or congestive heart failure.

L35 ANSWER 9 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 9  
 ACCESSION NUMBER: 2002:833548 HCAPLUS  
 DOCUMENT NUMBER: 137:334908  
 TITLE: Complement C4A biopolymer marker indicative of myocardial infarction and congestive heart failure having a molecular weight of 1896 daltons  
 INVENTOR(S): **Jackowski, George; Thatcher, Brad; Marshall, John; Yantha, Jason; Vrees, Tammy**  
 PATENT ASSIGNEE(S): Can.  
 SOURCE: U.S. Pat. Appl. Publ., 10 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2002161180 | A1   | 20021031 | US 2001-846343  | 20010430 |
| WO 2002088724 | A2   | 20021107 | WO 2002-CA612   | 20020426 |
| WO 2002088724 | A3   | 20030103 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-846343 A 20010430

AB The instant invention involves the use of a combination of preparatory steps in conjunction with **mass spectroscopy** and time-of-flight **detection** procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with ref. to their ability to evidence at least one particular disease state; thereby enabling a **diagnostician** to gain the ability to characterize either the presence or absence of said at least one disease state relative to recognition of the presence and/or the absence of said biopolymer. Serum samples were analyzed by SELDI-TOF using the Ciphergen PROTEINCHIP system and the disease specific marker identified by the sequence NGFKSHALQLNNRQIR and characterized as a complement C4A fragment having a mol. wt. of 1896 daltons was found. This marker is indicative of myocardial infarction, Type II diabetes, and congestive heart failure.

L35 ANSWER 10 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 10  
 ACCESSION NUMBER: 2002:833429 HCAPLUS  
 DOCUMENT NUMBER: 137:334903  
 TITLE: **Complement C3f** biopolymer marker



indicative of Type II diabetes having a molecular weight of 1998 daltons

INVENTOR(S): **Jackowski, George; Thatcher, Brad; Marshall, John; Yantha, Jason; Vrees, Tammy**

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 10 pp.  
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2002160532 | A1   | 20021031 | US 2001-846346  | 20010430 |
| WO 2002088707 | A2   | 20021107 | WO 2002-CA616   | 20020429 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-846346 A 20010430

AB The instant invention involves the use of a combination of preparatory steps in conjunction with **mass spectroscopy** and time-of-flight **detection** procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with ref. to their ability to evidence at least one particular disease state; thereby enabling a **diagnostician** to gain the ability to characterize either the presence or absence of said at least one disease state relative to recognition of the presence and/or the absence of said biopolymer. Serum samples were analyzed by SELDI-TOF using the Ciphergen PROTEINCHIP system and the disease specific marker identified by the sequence SSKITHRIHWESASLLR and characterized as a **complement C3f** fragment having a mol. wt. of 1998 daltons was found. This marker is indicative of Type II diabetes.

L35 ANSWER 11 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 11

ACCESSION NUMBER: 2002:833426 HCAPLUS

DOCUMENT NUMBER: 137:334902

TITLE: **Complement C3f** biopolymer marker  
indicative of myocardial infarction or congestive heart failure having a molecular weight of 1562 daltons

INVENTOR(S): **Jackowski, George; Thatcher, Brad; Vrees, Tammy; Yantha, Jason; Marshall, John**

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 10 pp.  
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2002160529 | A1   | 20021031 | US 2001-845738  | 20010430 |
| WO 2002088729 | A2   | 20021107 | WO 2002-CA629   | 20020429 |
| WO 2002088729 | A3   | 20021227 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-845738 A 20010430

AB The instant invention involves the use of a combination of preparatory steps in conjunction with **mass spectroscopy** and time-of-flight **detection** procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with ref. to their ability to evidence at least one particular disease state; thereby enabling a **diagnostician** to gain the ability to characterize either the presence or absence of said at least one disease state relative to recognition of the presence and/or the absence of said biopolymer. Serum samples were analyzed by SELDI-TOF using the Ciphergen PROTEINCHIP system and the disease specific marker identified by the sequence ITHRIHWESASLL and characterized as a **complement C3f** fragment having a mol. wt. of 1562 daltons was found. This marker is indicative of myocardial infarction or congestive heart failure.

L35 ANSWER 12 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 12

ACCESSION NUMBER: 2002:833402 HCAPLUS

DOCUMENT NUMBER: 137:334900

TITLE: **Complement C3f** biopolymer marker indicative of myocardial infarction and congestive heart failure having a molecular weight of 1777 daltons

INVENTOR(S): **Jackowski, George; Thatcher, Brad; Marshall, John; Yantha, Jason; Vrees, Tammy**

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 10 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2002160434 | A1   | 20021031 | US 2001-845735  | 20010430 |
| WO 2002088712 | A2   | 20021107 | WO 2002-CA628   | 20020429 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2001-845735 A 20010430

AB The instant invention involves the use of a combination of preparatory steps in conjunction with **mass spectroscopy** and time-of-flight **detection** procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with ref. to their ability to evidence at least one particular disease state; thereby enabling a **diagnostician** to gain the ability to characterize either the presence or absence of said at least one disease state relative to recognition of the presence and/or the absence of said biopolymer. Serum samples were analyzed by SELDI-TOF using the Ciphergen PROTEINCHIP system and the disease specific marker identified by the sequence SKITHRIHWESASLL and characterized as a **complement C3f** fragment having a mol. wt. of 1777 daltons was found. This marker is indicative of myocardial infarction, intracerebral hemorrhage, Type II diabetes, or congestive heart failure.

L35 ANSWER 13 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 13

ACCESSION NUMBER: 2002:833395 HCAPLUS

DOCUMENT NUMBER: 137:348834

TITLE: Process for **diagnosis** of physiological conditions by characterization of proteomic materials

INVENTOR(S): **Jackowski, George; Thatcher, Brad; Marshall, John; Yantha, Jason; Vrees, Tammy**

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 25 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2002160420 | A1   | 20021031 | US 2001-846330  | 20010430 |
| WO 2002088744 | A2   | 20021107 | WO 2002-CA623   | 20020429 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2001-846330 A 20010430

AB The present invention discloses the use of proteomic investigation as a **diagnostic** tool; and particularly teaches the use of proteomic investigative techniques and methodol. to det. a proteomic basis for the development and progression of abnormal physiol. conditions and the development and characterization of risk assessment, **diagnostic** and therapeutic means and methodologies. Serum samples from patients suffering from a variety of diseases in Syndrome X were analyzed by SELDI **mass spectrometry** using the Ciphergen PROTEINCHIP system to discern disease markers.

L35 ANSWER 14 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 14  
ACCESSION NUMBER: 2002:833394 HCAPLUS  
DOCUMENT NUMBER: 137:334897  
TITLE: **Complement C3f** biopolymer marker  
indicative of congestive heart failure having a  
molecular weight of 1793 daltons  
INVENTOR(S): **Jackowski, George; Thatcher, Brad;**  
**Marshall, John; Yantha, Jason;**  
**Vrees, Tammy**  
PATENT ASSIGNEE(S): Can.  
SOURCE: U.S. Pat. Appl. Publ., 10 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2002160419 | A1   | 20021031 | US 2001-845739  | 20010430 |
| WO 2002088725 | A2   | 20021107 | WO 2002-CA614   | 20020426 |
| WO 2002088725 | A3   | 20030103 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-845739 A 20010430

AB The instant invention involves the use of a combination of preparatory steps in conjunction with **mass spectroscopy** and time-of-flight **detection** procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with ref. to their ability to evidence at least one particular disease state; thereby enabling a **diagnostician** to gain the ability to characterize either the presence or absence of said at least one disease state relative to recognition of the presence and/or the absence of said biopolymer. Serum samples were analyzed by SELDI-TOF using the Ciphergen PROTEINCHIP system and the disease specific marker identified by the sequence SKITHRIHWESASLL and characterized as a **complement C3f** fragment having a mol. wt. of 1793 daltons was found. This marker is indicative of congestive heart failure.

L35 ANSWER 15 OF 87 HCAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2002:391912 HCAPLUS  
DOCUMENT NUMBER: 137:1836  
TITLE: Measurement of DNA methylation for analysis of the toxicology of substances  
INVENTOR(S): Olek, Alexander; Piepenbrock, Christian; Berlin, Kurt  
PATENT ASSIGNEE(S): Epigenomics Ag, Germany  
SOURCE: PCT Int. Appl., 113 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO.    | DATE     |
|------------------------|--|----------|--------------------|----------|
| WO 2002040710          | A2   | 20020523 | WO 2001-EP12951    | 20011108 |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                    |          |
| RW:                    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                    |          |
| DE 10056802            | A1   | 20020529 | DE 2000-10056802   | 20001114 |
| AU 2002023672          | A5   | 20020527 | AU 2002-23672      | 20011108 |
| PRIORITY APPLN. INFO.: |  |          | DE 2000-10056802 A | 20001114 |
|                        |  |          | WO 2001-EP12951 W  | 20011108 |

AB The invention relates to a method for anal. of the toxicol. of a substance by measuring its effects using changes in DNA methylation as an indicator of toxicol. According to the invention, a DNA sample is taken from an organism or a cell culture which has been exposed to a specific substance which is to be examd. on account of its toxicol. effect. The DNA contained in said sample is chem. pre-treated and the base sequence of a section of the modified DNA is detd. The preferred method is to convert cytosine in CpG dinucleotides to uracil using bisulfite. Probes specific for cytosine- or uracil-contg. DNA can be used to detect changes in methylation. From there, a characteristic methylation state or a characteristic methylation model is detd. for the sample. By comparison with data from methylation states of other samples, the effect of a substance on the organism or the cell culture is detd. and/or compared to other substances in toxicol. terms. A panel of sequences that can be used to analyze the effects of poisons is described.

L35 ANSWER 16 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:833396 HCAPLUS

DOCUMENT NUMBER: 137:307041

TITLE: Method for monitoring and validating stress induction of disease state

INVENTOR(S): **Jackowski, George**; Stanton, Eric B.

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 12 pp.  
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND   | DATE     | APPLICATION NO. | DATE     |
|---------------|--|----------|-----------------|----------|
| US 2002160421 | A1   | 20021031 | US 2001-846341  | 20010430 |
| WO 2002088709 | A2   | 20021107 | WO 2002-CA621   | 20020429 |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-846341 A 20010430

AB The present invention provides a biochem.-based methodol. for ascertaining the presence and/or verifying the historical release of biopolymers, which have been shown to be indicative of a disease state or are predictive of the development of said disease state. Serum samples from patients suffering from a variety of diseases were analyzed by SELDI **mass spectrometry** using the Ciphergen PROTEINCHIP system to discern disease markers. Congestive heart failure disease markers included a 1406 dalton serum albumin, a 1793 dalton **complement C3f**, and a 2056 dalton **complement C3f**.

L35 ANSWER 17 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 15

ACCESSION NUMBER: 2002:670594 HCAPLUS

TITLE: The gene expression fingerprint of human heart failure  
AUTHOR(S): Tan, Fen-Lai; Moravec, Christine S.; Li, Jianbo;  
Apperson-Hansen, Carolyn; McCarthy, Patrick M.; Young,  
James B.; Bond, Meredith

CORPORATE SOURCE: Department of Molecular Cardiology, Lerner Research  
Institute, Cleveland, OH, 44195, USA

SOURCE: Proceedings of the National Academy of Sciences of the  
United States of America (2002), 99(17), 11387-11392  
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Multiple pathways are responsible for transducing mech. and hormonal stimuli into changes in gene expression during heart failure. In this study our goals were (i) to develop a sound statistical method to establish a comprehensive cut off point for identification of differentially expressed genes, (ii) to identify a gene expression fingerprint for heart failure, (iii) to attempt to distinguish different etiologies of heart failure by their gene expression fingerprint, and (iv) to identify gene clusters that show coordinated up- or down-regulation in human heart failure. We used oligonucleotide microarrays to profile seven nonfailing (NF) and eight failing (F) human **hearts** with a **diagnosis** of end-stage dilated **cardiomyopathy**. Biol. and exptl. variability of the hybridization data were analyzed, and then a statistical anal. procedure was developed, including Student's test after log-transformation and Wilcoxon Mann-Whitney test. A comprehensive cutoff point composed of fold change, av. difference, and abs. call was then established and validated by TaqMan PCR. Of 6,606 genes on the GeneChip, 103 genes in 10 functional groups were differentially expressed between F and NF hearts. A dendrogram identified a gene expression fingerprint of F and NF hearts and also distinguished two F hearts with distinct etiologies (familial and alc. cardiomyopathy, resp.) with different expression patterns. K means clustering also revealed two potentially novel pathways assocd. with up-regulation of atrial natriuretic factor and brain natriuretic peptide and with increased expression of extracellular matrix proteins. Gene expression fingerprints may be useful indicators of heart failure etiologies.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 18 OF 87 MEDLINE DUPLICATE 16

ACCESSION NUMBER: 2002680757 MEDLINE

DOCUMENT NUMBER: 22328822 PubMed ID: 12441757

TITLE: Marked activation of complement and leukocytes and an increase in the concentrations of soluble endothelial adhesion molecules during cardiopulmonary resuscitation and early reperfusion after cardiac arrest in humans.  
AUTHOR: Bottiger Bernd W; Motsch Johann; Braun Volker; Martin Eike; Kirschfink Michael  
CORPORATE SOURCE: Department of Anesthesiology, University of Heidelberg, Germany.. bernd\_boettiger@med.uni-heidelberg.de  
SOURCE: CRITICAL CARE MEDICINE, (2002 Nov) 30 (11) 2473-80.  
Journal code: 0355501. ISSN: 0090-3493.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 200212  
ENTRY DATE: Entered STN: 20021121  
Last Updated on STN: 20021217  
Entered Medline: 20021211

AB OBJECTIVE: Animal studies have demonstrated that reperfusion disorders occurring after cardiac arrest affect outcome. Reperfusion injury can be caused by activation of complement, polymorphonuclear leukocytes (PMN), and PMN-endothelial interaction. We studied different specific markers of these processes during and after cardiopulmonary resuscitation in humans. DESIGN: Prospective clinical trial. SETTING: University hospital. PATIENTS: A total of 55 patients who underwent out-of-hospital cardiopulmonary resuscitation for nontraumatic causes. INTERVENTIONS: Blood samples were drawn immediately, 15 mins, and 30 mins after initiation of cardiopulmonary resuscitation. In the case of restoration of spontaneous circulation, additional blood samples were taken at serial time points until 7 days after **cardiac** arrest. **MEASUREMENTS AND MAIN RESULTS:** A marked activation of complement and PMN was found in all patients investigated. Serum concentrations of specific activation markers of the **complement** system, anaphylatoxin **C3a** and the soluble membrane attack complex SC5b-9, and PMN elastase were increased during cardiopulmonary resuscitation and for  $\leq 48$  hrs after restoration of spontaneous circulation. Compared with controls at 30 mins after initiation of cardiac massage, concentrations of C3a, SC5b-9, and PMN elastase were increased in patients without and in those with restoration of spontaneous circulation. PMN elastase concentrations were significantly greater in patients without restoration of spontaneous circulation than in those who could be stabilized. In addition, the plasma concentrations of the soluble P-selectin were significantly increased between 15 mins and 24 hrs after the start of cardiopulmonary resuscitation. The concentrations of soluble intercellular adhesion molecule-1 were increased between 2 hrs and 72 hrs. **CONCLUSIONS:** Our data clearly demonstrate a marked activation of complement and PMN and an increased PMN-endothelial interaction during cardiopulmonary resuscitation and early reperfusion after cardiac arrest in humans. These changes are known to induce reperfusion disorders and tissue injury and point to new therapeutic options to improve outcome after cardiac arrest.

L35 ANSWER 19 OF 87 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2002:535965 BIOSIS  
DOCUMENT NUMBER: PREV200200535965  
TITLE: Cerebral embolism complicating Libman-Sacks endocarditis: Full recovery using recombinant tissue plasminogen activator.  
AUTHOR(S): Joven, Beatriz (1); Mellor-Pita, Susana (1); D'Cruz, David

(1); Sharief, Mohammed (1); Khamashta, Munther (1); Hughes, Graham R. V. (1)  
 CORPORATE SOURCE: (1) Lupus Research Unit, The Rayne Institute, St. Thomas' Hospital, Lambeth Palace Road, London, SE1 7EH UK  
 SOURCE: Journal of Rheumatology, (September, 2002) Vol. 29, No. 9, pp. 2022-2024. <http://www.jrheum.com>. print.  
 ISSN: 0315-162X.  
 DOCUMENT TYPE: Article; Letter  
 LANGUAGE: English

L35 ANSWER 20 OF 87 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 ACCESSION NUMBER: 2002:609236 BIOSIS  
 DOCUMENT NUMBER: PREV200200609236  
 TITLE: Proteomic analysis of mouse C3 deficiency and liver partial hepatectomy.  
 AUTHOR(S): Strey, C. W. (1); Spellman, D. (1); Markiewski, M. (1); Lambris, J. D. (1)  
 CORPORATE SOURCE: (1) Laboratory of Protein Chemistry, Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA, 19104 USA  
 SOURCE: International Immunopharmacology, (August, 2002) Vol. 2, No. 9, pp. 1241. <http://www.elsevier.com/locate/intimp>. print.  
 Meeting Info.: XIX International Complement Workshop  
 Palermo, Italy September 22-26, 2002  
 ISSN: 1567-5769.  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

L35 ANSWER 21 OF 87 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2002:369923 HCAPLUS  
 DOCUMENT NUMBER: 137:351829  
 TITLE: Identification of low-abundance proteins of bovine colostrum and mature milk using two-dimensional electrophoresis followed by microsequencing and **mass spectrometry**  
 AUTHOR(S): Yamada, Masamichi; Murakami, Kouki; Wallingford, John C.; Yuki, Yoshikazu  
 CORPORATE SOURCE: JCR Pharmaceuticals Co., Ltd., Kobe, 651-2241, Japan  
 SOURCE: Electrophoresis (2002), 23(7-8), 1153-1160  
 CODEN: ELCTDN; ISSN: 0173-0835  
 PUBLISHER: Wiley-VCH Verlag GmbH  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The authors identified several low-abundance proteins of bovine colostrum and mature milk using the immunoabsorption technique and two-dimensional electrophoresis (2-DE) followed by microsequencing and **mass spectrometry**. Two major milk proteins, .beta.-casein and IgG (IgG), were effectively removed from the milk using immunoabsorbents. Milk samples before and after immunoabsorption were sepd. by 2-DE. Protein identification of the spots on 2-DE was performed by either gel comparison, microsequencing, matrix-assisted **laser desorption/ionization-time of flight mass-spectrometry** (MALDI-TOF-MS), peptide mass fingerprinting or peptide sequencing using tandem MS by hybrid quadrupole/orthogonal acceleration time of flight-MS (Q-TOF). Significant differences in protein patterns were obsd. between the low-abundance proteins of colostrum and mature milk. In addn., several low-abundance proteins including fibrinogen .beta.-chain, chitinase 3-like 1,



.alpha.-antitrypsin, **complement C3** .alpha.-chain, gelsolin and apolipoprotein H were obsd. only in colostrum. However, the level of .beta.-casein fragments increased significantly during this lactation period. .alpha.-Lactalbumin and .beta.-lactoglobulin as well as some low-abundance proteins including bovine serum albumin, serotransferrin and lactoferrin were identified in both colostrum and mature milk. Low-abundance proteins in bovine colostrum may have special physiol. relevance to the health and development of calves early in lactation.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 22 OF 87 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:413298 BIOSIS

DOCUMENT NUMBER: PREV200200413298

TITLE: Immunological analysis of pleural fluid in post-cardiac injury syndrome.

AUTHOR(S): Shrivastava, R. (1); Venkatesh, S.; Pavlovich, B. B.; Bharadwaj, J.; Vaz, A.

CORPORATE SOURCE: (1) Department of Internal Medicine, Park Ridge Hospital, 1555 Long Pond Road, Rochester, NY, 14626; rs243@hotmail.com USA

SOURCE: Postgraduate Medical Journal, (June, 2002) Vol. 78, No. 920, pp. 362-363. <http://www.postgradmedj.com>. print. ISSN: 0032-5473.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Post-cardiac injury syndrome (PCIS) is an inflammatory process involving pleura and pericardium secondary to cardiac injury. Even though this clinical entity has been recognised for decades, **diagnosis** is difficult because of lack of a **diagnostic** test. Antimyocardial antibody titre in pleural fluid and serum has been proposed to have **diagnostic** value. However, there are inherent difficulties in **measuring** and interpreting the role of antimyocardial antibody. A case of PCIS with low pleural fluid complement level is reported, which it is believed can be useful to support the **diagnosis** of PCIS.

L35 ANSWER 23 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002424460 EMBASE

TITLE: Predictors of allograft ischemic injury in clinical heart transplantation.

AUTHOR: Kjellman U.W.; Shariari A.; Svensson G.; Wiklund L.; Bengtsson A.; Ekroth R.

CORPORATE SOURCE: Dr. U.W. Kjellman, Dept. of Thoracic/Cardiovasc. Surg., Sahlgrenska University Hospital, SE-413 45 Goteborg, Sweden

SOURCE: Scandinavian Cardiovascular Journal, (2002) 36/5 (313-318). Refs: 10 ISSN: 1401-7431 CODEN: SCJOFY

COUNTRY: Norway

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery  
030 Pharmacology  
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Objectives - 1. Identify clinical, biochemical and inflammatory predictors of allograft ischemic injury in clinical heart transplantation. 2. Evaluate the impact of high dose insulin (GIK) on allograft metabolism during blood cardioplegia and post-ischemic injury. Design - A clinical,

prospective, randomized open trial comprising 25 consecutive heart transplantations at a university hospital. Ischemic injury was evaluated from plasma levels of creatine kinase isoenzyme MB (CK-MB). Blood cardioplegic arterial and coronary sinus concentrations of C3a, IL-6, substrates, amino acids and blood gases were **measured** at the end of the implantation period, prior to reperfusion. Twelve patients received high dose insulin with glucose, potassium and amino acids. Results - CK-MB increased from 1.9  $\pm$  0.2 to 161  $\pm$  13  $\mu$ g/l (range 47-293  $\mu$ g/l). The peak level of CK-MB correlated with donor age ( $r = 0.48$ ,  $p = 0.02$ ) and implantation time ( $r = 0.53$ ,  $p = 0.02$ ); and with recipient plasma IL-6 ( $r = 0.56$ ,  $p = 0.02$ ), allograft oxygen extraction ( $r = 0.56$ ,  $p = 0.02$ ), lactate release ( $r = 0.47$ ,  $p = 0.02$ ) and allograft arterial-coronary sinus (cs) pH ( $r = 0.47$ ,  $p = 0.02$ ) all during final cardioplegia before reperfusion. Seventy-two percent of the variance of CK-MB was explained by a model which included donor age, art-cs pH difference and arterial IL-6. In contrast, CK-MB was unrelated to total ischemic time ( $r = -0.17$ ,  $p = 0.38$ ). Insulin infusion had no effect on myocardial substrates during cardioplegia, or on post-ischemic CK-MB. Conclusion - Donor age, duration and quality of the implantation period are significant predictors of allograft ischemic injury in heart transplantation. High dose insulin had no **detectable** effects on allograft metabolism during **cardioplegia**, or on subsequent ischemic injury.

L35 ANSWER 24 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:333939 HCAPLUS

DOCUMENT NUMBER: 136:398115

TITLE: A proteomic approach for identification of secreted proteins during the differentiation of 3T3-L1 preadipocytes to adipocytes

AUTHOR(S): Kratchmarova, Irina; Kalume, Dario E.; Blagoev, Blagoy; Scherer, Philipp E.; Podtelejnikov, Alexandre V.; Molina, Henrik; Bickel, Perry E.; Andersen, Jens S.; Fernandez, Minerva M.; Bunkenborg, Jacob; Roepstorff, Peter; Kristiansen, Karsten; Lodish, Harvey F.; Mann, Matthias; Pandey, Akhilesh

CORPORATE SOURCE: Center for Experimental Bioinformatics, University of Southern Denmark, Odense M, DK-5230, Den.

SOURCE: Molecular and Cellular Proteomics (2002), 1(3), 213-222

CODEN: MCPOBS; ISSN: 1535-9476

PUBLISHER: American Society for Biochemistry and Molecular Biology, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have undertaken a systematic proteomic approach to purify and identify secreted factors that are differentially expressed in preadipocytes vs. adipocytes. Using one-dimensional gel electrophoresis combined with nanoelectrospray tandem **mass spectrometry**, proteins that were specifically secreted by 3T3-L1 preadipocytes or adipocytes were identified. In addn. to a no. of previously reported mols. that are up- or down-regulated during this differentiation process (adipsin, adipocyte complement-related protein 30 kDa, **complement C3**, and fibronectin), we identified four secreted mols. that have not been shown previously to be expressed differentially during the process of adipogenesis. Pigment epithelium-derived factor, a sol. mol. with potent antiangiogenic properties, was found to be highly secreted by preadipocytes but not adipocytes. Conversely, we found hippocampal cholinergic neurostimulating peptide, neutrophil gelatinase-assocd. lipocalin, and haptoglobin to be expressed highly by mature adipocytes.

We also used liq. chromatog.-based sepn. followed by automated tandem **mass spectrometry** to identify proteins secreted by mature adipocytes. Several addnl. secreted proteins including resistin, secreted acidic cysteine-rich glycoprotein/osteonectin, stromal cell-derived factor-1, cystatin C, gelsolin, and matrix metalloprotease-2 were identified by this method. To our knowledge, this is the first study to identify several novel secreted proteins by adipocytes by a proteomic approach using **mass spectrometry**.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 25 OF 87 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:516645 BIOSIS

DOCUMENT NUMBER: PREV200200516645

TITLE: The increased histamine release in ischaemic heart disease patients undergoing coronaroangiography is not mediated by specific IgE.

AUTHOR(S): Rodriguez, R. M. (1); Gueant, J.-L.; Aimone-Gastin, I.; Gerard, P.; Amoghly, F.; Bellou, A.; Julliere, Y.; Faure, G.; Danchin, N.; Romano, A.

CORPORATE SOURCE: (1) Laboratoire de Pathologie Cellulaire et Moleculaire en Nutrition, Faculte de Medecine, Equipe INSERM 0014, F-54505, BP 184, Vandoeuvre-les-Nancy Cedex France

SOURCE: Allergy (Copenhagen), (2002) Vol. 57, No. Supplement 72, pp. 61-66. <http://www.blackwellmunksgaard.com/allergy>. print.  
ISSN: 0105-4538.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Background: The release of histamine by iodinated contrast media (ICM) is higher in coronary artery disease patients than in noncoronary patients during coronary angiogram. Methods: Eighty-eight patients who underwent a coronary angiography were classified either as having coronary artery disease or as noncoronary patients. Histamine concentration was higher than the 6.8 nM upper limit in 7 cases (group 1), of whom six were coronary artery disease patients. We compared the IgE and complement fractions in plasma of these patients to two control groups with normal histamine blood level, one (group 2) with and the other (group 3) without coronary artery disease. Results: No difference of total IgE and **C3c** and **C4 complement** fractions was found among the three groups. Anti-ioxaglate IgE-RIA was positive in only one patient from group 1. The affinity of drug-IgE binding in the serum of this patient was very low (Kd: 18.7 mM). The level of anti-ICM IgE **detected** by ioxitalamate- and iomeprol-Sepharose RIA was significantly higher in groups 2 and 3 than in group 1. Conclusions: The higher histamine release in ischaemic heart disease patients undergoing coronaroangiography is not mediated by IgE or complement activation. Further studies are needed to investigate the implication of histamine release factors.

L35 ANSWER 26 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 17

ACCESSION NUMBER: 2001:798427 HCAPLUS

DOCUMENT NUMBER: 135:353806

TITLE: Human G protein-coupled receptor-like MOLX proteins and the nucleic acids that encode them

INVENTOR(S): Vernet, Corine A. M.; Fernandes, Elma R.; Gerlach, Valerie; Shimkets, Richard A.; Malyankar, Uriel M.; Boldog, Ferenc L.; Zerhusen, Bryan D.; Spytek, Kimberly A.; Majumder, Kumud; Tchernev, Velizar T.; Padigar, Muralidhara; Patturajan, Meera; Burgess,

Catherine E.; Gangolli, Esha A.; Smithson, Glennda;  
Rastelli, Luca; MacDougall, John R.; Taupier, Raymond  
J., Jr.; Grosse, William M.; Szekeres, Edward S., Jr.;  
Alsoborook, John P., II

PATENT ASSIGNEE(S): Curagen Corp., USA  
SOURCE: PCT Int. Appl., 227 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO. | DATE       |
|------------------------|--|----------|-----------------|------------|
| WO 2001081578          | A2   | 20011101 | WO 2001-US13578 | 20010426   |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |            |
| RW:                    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |          |                 |            |
| PRIORITY APPLN. INFO.: |  |          | US 2000-200158P | P 20000426 |
|                        |  |          | US 2000-200780P | P 20000428 |
|                        |  |          | US 2000-201006P | P 20000501 |
|                        |  |          | US 2000-201007P | P 20000501 |
|                        |  |          | US 2000-201236P | P 20000501 |
|                        |  |          | US 2000-201238P | P 20000502 |
|                        |  |          | US 2000-201474P | P 20000503 |
|                        |  |          | US 2000-201508P | P 20000503 |
|                        |  |          | US 2000-220591P | P 20000725 |
|                        |  |          | US 2000-232678P | P 20000915 |
|                        |  |          | US 2001-263217P | P 20010122 |
|                        |  |          | US 2001-265160P | P 20010130 |

AB Disclosed herein are 15 nucleic acid sequences that encode human G protein-coupled receptor-related polypeptides, designated MOL1 to MOL10b. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivs., variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. Nearest neighbor sequence homologies, protein domains, tissue expression profiles, and chromosomal location are also provided. The invention further discloses therapeutic, **diagnostic** and research methods for **diagnosis**, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

L35 ANSWER 27 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:618207 HCAPLUS

DOCUMENT NUMBER: 135:190398

TITLE: Nucleic acid markers useful for the identification, assessment, prevention and therapy of human cancers

INVENTOR(S): Roth, Frederick P.; Van Huffel, Christophe; White, James V.; Shyjan, Andrew W.

PATENT ASSIGNEE(S): Millennium Predictive Medicine, Inc., USA

SOURCE: PCT Int. Appl., 126 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.   | KIND | DATE  | APPLICATION NO. | DATE     |
|--|------|---|-----------------|----------|
| WO 2001061048  | A2   | 20010823  | WO 2001-US5263  | 20010216 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,<br>CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,<br>HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,<br>LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,<br>SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,<br>ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,<br>DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,<br>BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |      |   |                 |          |
| US 2002051978  | A1   | 20020502  | US 2001-788100  | 20010216 |
| PRIORITY APPLN. INFO.:   |      | US 2000-183312P P 20000217  |                 |          |
| AB The present invention is directed to the identification of markers that<br>can be used to det. the sensitivity of cancer cells to a therapeutic<br>agent. The present invention is also directed to the identification of<br>therapeutic targets. Nucleic acid arrays were used to det. the level of<br>expression of sequences (genes) found in 60 different solid tumor cancer<br>cell lines selected from the NCI 60 cancer cell line series. Expression<br>anal. was used to identify markers assocd. with sensitivity to certain<br>chemotherapeutic agents.   |      |   |                 |          |
| L35 ANSWER 28 OF 87 HCAPLUS COPYRIGHT 2003 ACS   |      |   |                 |          |
| ACCESSION NUMBER:  |      | 2001:411495 HCAPLUS   |                 |          |
| DOCUMENT NUMBER:   |      | 135:179631  |                 |          |
| TITLE:   |      | Profiling changes in gene expression during<br>differentiation and maturation of monocyte-derived<br>dendritic cells using both oligonucleotide microarrays<br>and proteomics |                 |          |
| AUTHOR(S):   |      | Le Naour, Francois; Hohenkirk, Lyndon; Grolleau,<br>Annabelle; Misek, David E.; Lescure, Pascal; Geiger,<br>James D.; Hanash, Samir; Beretta, Laura                           |                 |          |
| CORPORATE SOURCE:  |      | Department of Microbiology and Immunology, University<br>of Michigan, Ann Arbor, MI, 48109-0666, USA  |                 |          |
| SOURCE:  |      | Journal of Biological Chemistry (2001), 276(21),<br>17920-17931<br>CODEN: JBCHA3; ISSN: 0021-9258   |                 |          |
| PUBLISHER:   |      | American Society for Biochemistry and Molecular<br>Biology  |                 |          |
| DOCUMENT TYPE:   |      | Journal   |                 |          |
| LANGUAGE:  |      | English   |                 |          |
| AB Dendritic cells (DCs) are antigen-presenting cells that play a major role<br>in initiating primary immune responses. The authors have utilized two<br>independent approaches, DNA microarrays and proteomics, to analyze the<br>expression profile of human CD14+ blood monocytes and their derived DCs.<br>Anal. of gene expression changes at the RNA level using oligonucleotide<br>microarrays complementary to 6300 human genes showed that .apprx.40% of<br>the genes were expressed in DCs. A total of 255 genes (4%) were regulated<br>during DC differentiation or maturation. Most of these genes were not<br>previously assocd. with DCs and included genes encoding secreted proteins<br>as well as genes involved in cell adhesion, signaling, and lipid metab.<br>Protein anal. of the same cell populations was done using two-dimensional<br>gel electrophoresis. A total of 900 distinct protein spots were included,<br>and 4% of them exhibited quant. changes during DC differentiation and |      |   |                 |          |

maturation. Differentially expressed proteins were identified by **mass spectrometry** and found to represent proteins with  $\text{Ca}^{2+}$  binding, fatty acid binding, or chaperone activities as well as proteins involved in cell motility. In addn., proteomic anal. provided an assessment of post-translational modifications. The chaperone protein, calreticulin, was found to undergo cleavage, yielding a novel form. The combined oligonucleotide microarray and proteomic approaches have uncovered novel genes assocd. with DC differentiation and maturation and has allowed anal. of post-translational modifications of specific proteins as part of these processes.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 29 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001223124 EMBASE

TITLE: Hemodynamic consequences of porcine kidney xenograft reperfusion in cynomolgus monkeys.

AUTHOR: Przemeck M.; Vangerow B.; Loss M.; Schmidtko J.; Klemptner J.; Ruckoldt H.; Piepenbrock S.; Winkler M.

CORPORATE SOURCE: Dr. M. Przemeck, Abt. Anas-thesiologie I, Medizinische Hochschule Hannover, 30623 Hannover, Germany

SOURCE: Transplantation, (15 Jun 2001) 71/11 (1512-1514).

Refs: 11

ISSN: 0041-1337 CODEN: TRPLAU

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery

026 Immunology, Serology and Transplantation

028 Urology and Nephrology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Background. After xenograft reperfusion, complement activation may lead to generation of anaphylatoxins and cardiocirculatory instability of the recipient. Methods. In 13 cynomolgus recipients of either unmodified or human decay accelerating factor transgenic porcine kidneys **cardiocirculatory** parameters were **measured** by single indicator transpulmonary thermodilution. Results. After graft reperfusion, recipient cardiac output decreased by 25.4% ( $P < 0.05$ ), intrathoracic blood volume by 22.8% ( $P < 0.05$ ), extravascular lung water increased slightly ( $P = \text{n.s.}$ ). The impairment in cardiac output was neither influenced by the graft's weight or human decay accelerating factor transgenicity. sC3a and sC5b-9 complement levels in the recipient monkeys showed a sharp peak upon reperfusion. Conclusions. After reperfusion a marked and significant cardiodepression accompanied by relative volume depletion were observed. Analysis of volume status ruled out a mere volume shift as the underlying reason for the observed drop in cardiac output. These data may be relevant for the perioperative management of human recipients of discordant xenografts in the future.

L35 ANSWER 30 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:351349 HCAPLUS

DOCUMENT NUMBER: 136:149462

TITLE: Cloning and purification of the rainbow trout fifth component of complement (C5)

AUTHOR(S): Franchini, S.; Zarkadis, I. K.; Sfyroera, G.; Sahu, A.; Moore, W. T.; Mastellos, D.; LaPatra, S. E.; Lambris, J. D.

CORPORATE SOURCE: 401 Stellar-Chance Laboratories, Department of Pathology and Laboratory Medicine, University of

SOURCE: Pennsylvania, Philadelphia, PA, 19104, USA  
 Developmental & Comparative Immunology (2001),  
 25(5-6), 419-430  
 CODEN: DCIMDQ; ISSN: 0145-305X  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB To gain further insight into the evolutionary history of the  
**complement** proteins C3, C4, and C5 we have now cloned  
 the fifth component of complement from a rainbow trout (*Oncorhynchus*  
*mykiss*) liver cDNA library; this is the first report of C5 cloning in a  
 species other than human and mouse. The deduced amino acid sequence of a  
 partial cDNA clone (2.25 kb), representing approx. 44% of the coding  
 sequence, showed 60 and 58% similarity to human and mouse C5, resp. To  
 validate the mol. information derived from the cloning we developed an  
 improved purifn. protocol. **Mass spectrometric** anal.  
 of C5 tryptic digests yielded peptide signals that matched theor. protein  
 sequence derived from the partial cDNA. Northern blot anal. of RNA from  
 various tissues showed the presence of a single mRNA transcript in trout  
 liver and Southern blot anal. indicated that the gene coding for C5 is  
 present as a single copy in the trout genome. The presence of C5 in trout  
 suggests that C3, C4, and C5 must have diverged before the appearance of  
 teleost fish.  
 REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT  
 L35 ANSWER 31 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 2002004406 EMBASE  
 TITLE: A proteomic approach for the discovery of early  
**detection** markers of hepatocellular carcinoma.  
 AUTHOR: Steel L.F.; Mattu T.S.; Mehta A.; Hebestreit H.; Dwek R.;  
 Evans A.A.; London W.T.; Block T.  
 CORPORATE SOURCE: T. Block, Department of Biochemistry, Jefferson Ctr. for  
 Biomedical Res., Thomas Jefferson University, Doylestown,  
 PA 18901, United States. tim.block@mail.tju.edu  
 SOURCE: Disease Markers, (2001) 17/3 (179-189).  
 Refs: 56  
 ISSN: 0278-0240 CODEN: DMARD3  
 COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 004 Microbiology  
 016 Cancer  
 017 Public Health, Social Medicine and Epidemiology  
 048 Gastroenterology  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 AB Individuals chronically infected with hepatitis B or C virus (HBV, HCV)  
 are at high risk for the development of hepatocellular carcinoma (HCC),  
 with disease progression occurring relentlessly over many years. The  
**diagnosis** of HCC usually occurs at late stages in the disease when  
 there are few effective treatment options and the prognosis for patients  
 with HCC is very poor. The long latency period, together with clearly  
 identified at risk populations, provide opportunities for earlier  
**detection** that will allow more timely and effective treatment of  
 this devastating cancer. We are using a proteomic approach to test the  
 hypothesis that changes in the amount of certain serum polypeptides, or  
 changes in their post-translational modifications, can be used to predict  
 the onset of HCC. Advances in the standardization of two dimensional gel  
 electrophoresis (2DE) coupled with computerized image analysis now permit

the reproducible resolution of thousands of polypeptides per run. Serum polypeptides from individuals at different stages in the disease continuum are being resolved by 2DE to identify those that change with disease progression. Polypeptides found by this method can be further characterized by **mass spectrometry**. In addition, the potential for changes in the glycan structure of certain polypeptides to serve as a marker for disease progression can be explored. The proteomic approach is expected to liberate us from the need to "cherry pick" or guess the best biomarkers and let the data tell us which are the best indicators of disease. Information may also be gleaned about the pathobiology of the disease process.

L35 ANSWER 32 OF 87 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2001:105315 HCAPLUS  
 DOCUMENT NUMBER: 134:249174  
 TITLE: Towards defining the urinary proteome using liquid chromatography-tandem **mass spectrometry**. I. Profiling an unfractionated tryptic digest  
 AUTHOR(S): Spahr, Chris S.; Davis, Michael T.; McGinley, Michael D.; Robinson, John H.; Bures, Edward J.; Beierle, Jill; Mort, Jessica; Courchesne, Paul L.; Chen, Kui; Wahl, Robert C.; Yu, Wen; Luethy, Roland; Patterson, Scott D.  
 CORPORATE SOURCE: Departments of Biochemistry and Genetics, Thousand Oaks, CA, USA  
 SOURCE: Proteomics (2001), 1(1), 93-107  
 Published in: Electrophoresis, 22(2)  
 CODEN: PROTC7; ISSN: 1615-9853  
 PUBLISHER: Wiley-VCH Verlag GmbH  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The proteome of normal male urine from a com. pooled source has been examd. using direct liq. chromatog.-tandem **mass spectrometry** (LC-MS/MS). The entire urinary protein mixt. was denatured, reduced and enzymically digested prior to LC-MS/MS anal. using a hybrid-quadrupole time-of-flight **mass spectrometer** (Q-TOF) to perform data-dependent ion selection and fragmentation. To fragment as many peptides as possible, the mixt. was analyzed four sep. times, with the **mass spectrometer** selecting ions for fragmentation from a subset of the entire mass range for each run. This approach requires only an autosampler on the HPLC for automation (i.e, unattended operation). Across these four analyses, 1.450 peptide MS/MS spectra were matched to 751 sequences to identify 124 gene products (proteins and translations of expressed sequence tags). Interestingly, the exptl. time for these analyses was less than that required to run a single two-dimensional gel.  
 REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 33 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 2001098832 EMBASE  
 TITLE: A primate model for discordant pig to primate kidney xenotransplantation without hyperacute graft rejection.  
 AUTHOR: Loss M.; Schmidtko J.; Przemeck M.; Kunz R.; Arends H.; Jalali A.; Lorenz R.; Piepenbrock S.; Klempnauer J.; Winkler M.  
 CORPORATE SOURCE: Dr. M. Winkler, Klin. Viszeral/Transplantationschir., Medizinische Hochschule, Carl Neuberg Str. 1, 30625



SOURCE: Hannover, Germany. Winkler@tx-amb.mh-hannover.de  
Journal of Investigative Surgery, (2001) 14/1 (21-29).  
Refs: 22  
ISSN: 0894-1939 CODEN: JISUE5

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
009 Surgery  
026 Immunology, Serology and Transplantation  
028 Urology and Nephrology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Organs transplanted between phylogenetically disparate species, such as from the pig into the primate, are subject to intragraft deposition of preformed recipient immunoglobulin M (IgM) antibodies with subsequent complement activation finally leading to complete and rapid destruction of the xenograft (hyperacute graft rejection, HAR). Current therapeutic strategies for abrogation of HAR include pretransplant antibody absorption by specific or nonspecific extracorporeal column perfusion, ex vivo donor organ perfusion, the administration of substances interfering with complement activation, or even the genetic alteration of the donor. Here, in the pig to cynomolgus monkey species combination, we are describing an experimental model for abrogation of HAR by using large, relative to the recipient weight, oversized donor kidneys as xenotransplants. Porcine kidney xenotransplantation (n = 15) was performed using large white pigs of different weights and ages as organ donors and cynomolgus monkeys as recipients. In grafts with an organ weight below 50 g (20 to 48 g, median 25 g), primary nonfunction (PNF) of the porcine kidney was observed in 11 out of 12 cases and complete HAR in 5 out of 12 experiments. In contrast, none of three grafts with a donor organ weight > 70 g showed signs of HAR or PNF. In one animal, a second porcine kidney from the same donor (23 g) was successfully transplanted immediately after HAR and subsequent removal of a first porcine kidney (20 g). By using appropriate immunohistochemistry stainings of reperfusion biopsies, profound deposition of recipient natural antibodies in both small and large xenografts was shown, with only scarce deposition of C3 and C5b-9 in the latter, indicating only incomplete intragraft activation of the complement cascade in these organs. Intraoperative **cardiac** output (CO) **measurements** performed in 7 experiments demonstrated a 20 to 50% decrease in CO following reperfusion in 6 out of 7 grafts irrespective of the donor organ weight. The intraoperative decrease in CO was not associated with perioperative morbidity or mortality. The use of oversized donor kidneys can enable the study of a variety of immunologic and physiologic sequela beyond HAR associated with life-supporting discordant primate kidney transplantation.

L35 ANSWER 34 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:514757 HCAPLUS

DOCUMENT NUMBER: 133:236142

TITLE: Phenotyping apolipoprotein E\*3-Leiden transgenic mice by two-dimensional polyacrylamide gel electrophoresis and **mass spectrometric** identification

AUTHOR(S): Skehel, J. Mark; Schneider, Klaus; Murphy, Nuala; Graham, Annette; Benson, G. Martin; Cutler, Paul; Camilleri, Patrick

CORPORATE SOURCE: Department of Analytical Sciences, SmithKline Beecham Pharmaceuticals, Essex, UK

SOURCE: Electrophoresis (2000), 21(12), 2540-2545

CODEN: ELCTDN; ISSN: 0173-0835

PUBLISHER: Wiley-VCH Verlag GmbH  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Apolipoprotein E (ApoE) plays an important role in cholesterol and triglyceride metab., being one of the major structural components of chylomicrons and very low d. lipoprotein (VLDL) remnants. ApoE functions as a ligand in the receptor-mediated uptake of these remnants from the blood by the liver. A variant form of ApoE, apolipoprotein E\*3-Leiden, shows reduced affinity for the low d. lipoprotein (LDL) receptor, and results in the dominant expression of type III hyperlipoproteinemia. Two-dimensional electrophoresis (2-DE) has been used to characterize protein expression in serum samples from control and transgenic mice expressing the human ApoE\*3-Leiden mutation, fed a cholesterol-rich diet, and transgenic mice fed a normal diet. For the identification of proteins, single silver-stained spots were excised from the 2-DE gels and subjected to in-gel enzymic digestion. Extd. peptides were analyzed by matrix-assisted **laser desorption** ionization time-of-flight **mass spectrometry** (MALDI-TOF-MS). This proteomic approach has enabled the ApoE\*3-Leiden variant to be positioned in a 2-DE sepn. of serum proteins, and has identified changes in the expression of haptoglobin, indicating that this protein may provide a marker for the potential onset of atherosclerosis.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 35 OF 87 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
18

ACCESSION NUMBER: 2000:403018 BIOSIS

DOCUMENT NUMBER: PREV200000403018

TITLE: Identification of two-dimensionally separated human cerebrospinal fluid proteins by N-terminal sequencing, matrix-assisted **laser desorption** /ionization - **mass spectrometry**, nanoliquid chromatography-electrospray ionization-time of flight-**mass spectrometry**, and tandem **mass spectrometry**.

AUTHOR(S): Raymackers, Jos; Daniels, Annick; De Brabandere, Veronique (1); Missiaen, Carla; Dauwe, Martine; Verhaert, Peter; Vanmechelen, Eugene; Meheus, Lydie

CORPORATE SOURCE: (1) Department of Protein Analysis, Innogenetics NV, Industriepark Zwijnaarde 7, B-9052, Zwijnaarde Belgium

SOURCE: Electrophoresis, (June, 2000) Vol. 21, No. 11, pp. 2266-2283. print.  
ISSN: 0173-0835.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Optimal application of biological **mass spectrometry** (MS) in combination with two-dimensional polyacrylamide gel electrophoresis (2-D PAGE) of human cerebrospinal fluid (CSF) can lead to the identification of new potential biological markers of neurological disorders. To this end, we analyzed a number of 2-D PAGE protein spots in a human CSF pool using spot co-localization, N-terminal sequencing, matrix-assisted **laser desorption/ionization-mass spectrometry** (MALDI-MS) and nanoliquid chromatography-electrospray ionization-time of flight-**mass spectrometry** (nanoLC-ESI-TOF-MS) with tandem MS switching. Our constructed CSF master contained 469 spots after image analysis and

processing of 2-D gels. Upon visual inspection of our CSF master with the CSF pattern available on the ExPASy server, it was possible to locate and annotate 15 proteins. N-terminal sequence analysis and MALDI-MS peptide mass fingerprint analysis of both silver- and Coomassie Brilliant Blue (CBB) G-250-stained protein spots after in situ trypsin digest not only confirmed nine of the visually annotated spots but additionally resolved the identity of another 13 spots. Six of these proteins were not annotated on the 2-D ExPASy map: **complement C3** alpha-chain (1321-1663), complement factor B, cystatin C, calgranulin A, hemoglobin beta-chain, and beta-2-microglobulin. It was clear that MALDI-MS identification from CBB G-250-stained, rather than from silver-stained, spots was more successful. In cases where no N-terminal sequence and/or no clear MALDI-MS result was available, nanoLC-ESI-TOF-MS and tandem MS automated switching was used to clarify and/or identify these protein spots by generating amino acid sequence tags. In addition, enrichment of the concentration of low-abundant proteins on 2-D PAGE was obtained by removal of albumin and immunoglobulins from the CSF pool using affinity chromatography. Subsequent analysis by 2-D PAGE of the fractionated CSF pool showed various new silver-stainable protein spots, of which four were identified by nanoLC-ESI-TOF-MS and tandem MS switching. No significant homology was found in either protein or DNA databases, indicating that these spots were unknown proteins.

L35 ANSWER 36 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 19  
 ACCESSION NUMBER: 2000:379237 HCAPLUS  
 DOCUMENT NUMBER: 133:133838  
 TITLE: **Detection** of complement-fixing antiphospholipid antibodies in association with thrombosis  
 AUTHOR(S): Munakata, Yasuhiko; Saito, Takako; Matsuda, Kumiko; Seino, Jin; Shibata, Shinobu; Sasaki, Takeshi  
 CORPORATE SOURCE: Department of Clinical and Laboratory Medicine, Tohoku University School of Medicine, Sendai, 980-8574, Japan  
 SOURCE: Thrombosis and Haemostasis (2000), 83(5), 728-731  
 CODEN: THHADQ; ISSN: 0340-6245  
 PUBLISHER: F. K. Schattauer Verlagsgesellschaft mbH  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Antiphospholipid antibody (aPL) is a hallmark of antiphospholipid syndrome (APS), characterized by thrombosis and recurrent fetal loss. We developed a novel ELISA system to **detect** complement-fixing ability of anticardiolipin antibody (aCL), and evaluated its clin. usefulness through studying the prevalence of the antibodies in rheumatic diseases, esp. in assocn. with thrombosis and recurrent abortion. Among 189 patients with rheumatic diseases, the complement-fixing aCL was pos. in 26 (83.9%) of 31 patients with APS and 2 (1.3%) of 158 with other disease categories, whereas it was not pos. among 52 normal subjects. Twenty-seven of 28 patients (96.4%), who were pos. for complement-fixing aCL, had the episodes or history of thrombosis and/or recurrent abortion, at the time we studied. The remaining one in this group developed APS manifesting pulmonary infarction and occlusion of mesenteric artery 6 mo after the evaluation. The sensitivity and specificity of this **assay** system were 75.0% and 99.3%, resp., in relation with thrombotic episodes. On the other hand, the IgG aCL were pos. in 28 (77.8%) of 36 cases with recent thrombotic episodes and 24 (15.7%) of 153 cases with no recent thrombotic episodes. The sensitivity and specificity of IgG aCL **assay** system were 77.8% and 84.3%, resp., in relation with thrombotic episodes. These results indicate that complement-fixing aCL may specifically occur in assocn. with the episodes of thrombosis and/or

recurrent abortion in patients with APS compared to IgG-aCL. The method for **detecting** the complement-fixing aCL is simple, and it provides the useful **diagnostic** marker for thrombotic manifestations assocd. with APS.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 37 OF 87 MEDLINE

ACCESSION NUMBER: 2001305975 MEDLINE  
DOCUMENT NUMBER: 20562646 PubMed ID: 11112063  
TITLE: Prevention of hyperacute xenograft rejection in orthotopic xenotransplantation of pig hearts into baboons using immunoadsorption of antibodies and complement factors.  
AUTHOR: Brenner P; Reichenspurner H; Schmoeckel M; Wimmer C; Rucker A; Eder V; Meiser B; Hinz M; Felbinger T; Hammer C; Reichart B  
CORPORATE SOURCE: Department of Cardiac Surgery, Klinikum Grosshadern, Ludwig-Maximilians-University of Munich, Germany.. Paolo.Brenner@hch.med.uni-muenchen.de  
SOURCE: TRANSPLANT INTERNATIONAL, (2000) 13 Suppl 1 S508-17. Journal code: 8908516. ISSN: 0934-0874.  
PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200105  
ENTRY DATE: Entered STN: 20010604  
Last Updated on STN: 20010604  
Entered Medline: 20010531

AB To prevent hyperacute xenograft rejection (HXR) caused by preformed natural antibodies (XNAb) after orthotopic heart xenotransplantation (oXHTx) of landrace pig hearts into baboons, we used immunoadsorption of immunoglobulins IgG, IgM and IgA and complement with the reusable Ig-Therasorb column. In addition to functional data, tissue was sampled for histological, immunohistochemical and electron microscopical analysis. We performed three oXHTx of landrace pig hearts to baboons using extracorporeal circulation (ECC) connected to the immunoadsorption unit. Intraoperative treatment consisted of four cycles of immunoabsorption (IA). One oXHTx of a baboon without IA served as a control. A mismatch of donor and recipient heart size was prevented by selecting a 30-40% lower body weight of donor pigs than recipients. Four cycles of IA removed more than 80% of IgG, IgM and IgA, 86% of antipig antibodies and 66% of **complement** factors C3 and C4 from plasma. The graft of the control animal failed after 29 min. Orthotopic xenotransplantation with IA was selectively terminated after 100 min, 11 h and 21 h, respectively without any histological signs of HXR in light and electron microscopy. After weaning off from ECC these donor xenografts showed sufficient function with normal ECG and excellent **cardiac** output in echocardiography and invasive **measurement** (1.93 +/- 0.035 l/min). The myocardium of the control xenograft demonstrated more deposits of Ig and **complement** components (C3, C4) than in the IA group. Baboons survive HXR after orthotopic pig heart xenotransplantation due to antibody depletion by reusable Ig-Therasorb column treatment. Long-term survival in an orthotopic baboon xenotransplantation model after IA, especially in combination with transgenic pig organs, could be a reliable preclinical trial for future clinical xenotransplantation programs.

L35 ANSWER 38 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000092079 EMBASE  
TITLE: **Detection** of complement factor B in the cerebrospinal fluid of patients with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy disease using two-dimensional gel electrophoresis and **mass spectrometry**.  
AUTHOR: Unlu M.; De Lange R.P.J.; De Silva R.; Kalaria R.; St. Clair D.  
CORPORATE SOURCE: D. St. Clair, Department of Mental Health, Polwarth Building, University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD, United Kingdom. d.stclair@abdn.ac.uk  
SOURCE: Neuroscience Letters, (24 Mar 2000) 282/3 (149-152).  
Refs: 7  
ISSN: 0304-3940 CODEN: NELED5  
PUBLISHER IDENT.: S 0304-3940(00)00875-2  
COUNTRY: Ireland  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 008 Neurology and Neurosurgery  
022 Human Genetics  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a hereditary condition with onset in mid-adulthood and is associated with mutations in the Notch-3 gene. (Joutel, A., Corepechot, C., Ducros, A., Vahedi, K., Chabriat, H., Mouton, P., Alamowitch, S., Domenda, V., Cecilion, M., Marechal, J., Vayssiere, C., Cruaud, C., Cabanis, E.A., Ruchoux, M.M., Weissenbach, J., Bach, J.F., Bousser, M.G. and Tournier-Lasserre, E., Notch3 mutations in CADASIL, a hereditary adult-onset condition causing stroke and dementia. Nature, 383 (1996) 707-710) Ultrastructural examination of the pathology of the cerebral infarcts reveals deposits in the vascular smooth muscle cells of the small arteries of the brain, but there is no obvious indication how the Notch-3 mutations give rise to the observed pathology, nor is there any information on the exact nature of the deposits. We have investigated cerebrospinal fluid (CSF) from three CADASIL cases with known mutations in Notch-3 using two-dimensional gel electrophoresis. CSF from these patients was compared to that of six controls. We **detected** a single spot in the protein maps of patients which was absent from all the controls. In-gel tryptic digestion of this protein followed by **mass spectrometric** analysis of the tryptic fragments and a database search identified the spot as human complement factor B. These preliminary findings suggest that the alternative complement pathway may play a role in the pathogenesis of CADASIL. (C) 2000 Published by Elsevier Science Ireland Ltd.

L35 ANSWER 39 OF 87 HCAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 1999:813787 HCAPLUS  
DOCUMENT NUMBER: 132:121303  
TITLE: Identification of the C3b binding site in a recombinant vWF-A domain of complement factor B by surface-enhanced **laser desorption** -ionisation affinity **mass spectrometry** and homology modelling: Implications for the activity of factor B  
AUTHOR(S): Hinshelwood, Justin; Spencer, Daniel I. R.; Edwards, Yvonne J. K.; Perkins, Stephen J.  
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Royal Free and University College Medical School, London, NW3 2PF, UK

SOURCE: Journal of Molecular Biology (1999), 294(2), 587-599  
 CODEN: JMOBAK; ISSN: 0022-2836  
 PUBLISHER: Academic Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Factor B is a key component of the alternative pathway of the complement system. During complement activation, factor B complexed with activated C3 is cleaved into the Ba and Bb fragments by the protease factor D to form the C3 convertase from the complex between C3b and Bb. The Ba fragment contains three short consensus/complement repeat (SCR) domains, and the Bb fragment contains a von Willebrand factor type A (vWF-A) domain and a serine protease (SP) domain. Surface-enhanced **laser desorption-ionization affinity mass spectrometry** (SELDIAMS) was used to investigate the reaction of factor B with immobilized activated C3(NH3) in the presence of Mg<sup>2+</sup>. A recombinant vWF-A domain (residues G229-Q448), the native Ba and Bb fragments and native factor B all demonstrated specific interactions with C3(NH3), while no interactions were detected using bovine serum albumin as a control. A mass anal. of the proteolysis of the vWF-A domain when this was bound to immobilized C3(NH3) identified two peptides (residues G229-K265 and T355-R381) that were involved with vWF-A binding to C3(NH3). A homol. model for the vWF-A domain was constructed using the vWF-A crystal structure in complement receptor type 3. Comparisons with five different vWF-A crystal structures showed that large surface insertions were present close to the carboxyl and amino edges of the central .beta.-sheet of the factor B vWF-A structure. The peptides G229-K265 and T355-R381 corresponded to the two sides of the active site cleft at the carboxyl edge of the vWF-A structure. The vWF-A connections with the SCR and SP domains were close to the amino edge of this vWF-A .beta.-sheet, and shows that the vWF-A domain can be involved in both C3b binding and the regulation of factor B activity. These results show that (i) a major function of the vWF-A domain is to bind to activated C3 during the formation of the C3 convertase, which it does at its active site cleft; and that (ii) SELDIAMS provides an efficient means of identifying residues involved in protein-protein interactions. (c) 1999 Academic Press.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 40 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 1999142211 EMBASE  
 TITLE: Composition of the peptide fraction in human blood plasma: Database of circulating human peptides.  
 AUTHOR: Richter R.; Schulz-Knappe P.; Schrader M.; Standker L.; Jurgens M.; Tammen H.; Forssmann W.-G.  
 CORPORATE SOURCE: R. Richter, Lower Saxony Inst. Peptide Res., Feodor-Lynen-Strasse 31, D-30625 Hannover, Germany  
 SOURCE: Journal of Chromatography B: Biomedical Sciences and Applications, (1999) 726/1-2 (25-35).  
 Refs: 32  
 ISSN: 0378-4347 CODEN: JCBBEF  
 PUBLISHER IDENT.: S 0378-4347(99)00012-2  
 COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 025 Hematology  
 027 Biophysics, Bioengineering and Medical Instrumentation  
 029 Clinical Biochemistry  
 037 Drug Literature Index  
 LANGUAGE: English

## SUMMARY LANGUAGE: English

AB A database was established from human hemofiltrate (HF) that consisted of a mass database and a sequence database, with the aim of analyzing the composition of the peptide fraction in human blood. To establish a mass database, all 480 fractions of a peptide bank generated from HF were analyzed by MALDI-TOF **mass spectrometry**. Using this method, over 20 000 molecular masses representing native, circulating peptides were **detected**. Estimation of repeatedly **detected** masses suggests that approximately 5000 different peptides were recorded. More than 95% of the **detected** masses are smaller than 15 000, indicating that HF predominantly contains peptides. The sequence database contains over 340 entries from 75 different protein and peptide precursors. 55% of the entries are fragments from plasma proteins (fibrinogen A 13%, albumin 10%, .beta.2-microglobulin 8.5%, cystatin C 7%, and fibrinogen B 6%). Seven percent of the entries represent peptide hormones, growth factors and cytokines. Thirty-three percent belong to protein families such as complement factors, enzymes, enzyme inhibitors and transport proteins. Five percent represent novel peptides of which some show homology to known peptide and protein families. The coexistence of processed peptide fragments, biologically active peptides and peptide precursors suggests that HF reflects the peptide composition of plasma. Interestingly, protein modules such as EGF domains (meprin A.alpha.-fragments), somatomedin-B domains (vitronectin fragments), thyroglobulin domains (insulin like growth factor-binding proteins), and Kazal-type inhibitor domains were identified. Alignment of sequenced fragments to their precursor proteins and the analysis of their cleavage sites revealed that there are different processing pathways of plasma proteins in vivo. Copyright (C) 1999 Elsevier Science B.V.

L35 ANSWER 41 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:442424 HCAPLUS

DOCUMENT NUMBER: 129:79498

TITLE: Proteins of rat serum. Part 1. Establishing a reference two-dimensional electrophoresis map by immunodetection and microbore high performance liquid chromatography-electrospray **mass spectrometry**

AUTHOR(S): Haynes, Paul; Miller, Ingrid; Aebersold, Ruedi; Gemeiner, Manfred; Eberini, Ivano; Lovati, Maria Rosa; Manzoni, Cristina; Vignati, Mara; Gianazza, Elisabetta

CORPORATE SOURCE: Dep. Molecular Biotechnol., School Medicine, Univ. Washington, Seattle, WA, USA

SOURCE: Electrophoresis (1998), 19(8-9), 1484-1492

CODEN: ELCTDN; ISSN: 0173-0835

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have identified 56 major spots, or spot rows, corresponding to 22 proteins, in the 2-DE pattern of adult male rats. This was done mainly by applying 2 complementary techniques, namely immunoblotting and high performance liq. chromatog.-**mass spectrometry** (HPLC-MS) peptide mapping. Glycoproteins were characterized by affinity blotting with 6 lectins. The authors have detailed how rat blood serum differs from human serum in 2 main respects: (i) relative abundance of individual proteins, which amts. in some cases to a complete absence in either sample, and (ii) varying mol. parameters for homologous proteins. It was thus possible to establish a 1st-generation ref. map of rat serum proteins, which can be accessed through <http://Wb.u.washington.edu/.apprx.ruedilab/aeber-sold.html>. The recognition of species-specific proteins

appears of special relevance in this respect.

L35 ANSWER 42 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 20  
ACCESSION NUMBER: 1998361997 EMBASE  
TITLE: Human heart generates complement proteins that are upregulated and activated after myocardial infarction.  
AUTHOR: Yasojima K.; Schwab C.; McGeer E.G.; McGeer P.L.  
CORPORATE SOURCE: Dr. P.L. McGeer, Kinsmen Lab. of Neurol. Research, University of British Columbia, 2255 Wesbrook Mall, Vancouver, BC V6T 1Z3, Canada. mcgeerpl@unixg.ubc.ca  
SOURCE: Circulation Research, (19 Oct 1998) 83/8 (860-869).  
Refs: 46  
ISSN: 0009-7330 CODEN: CIRUAL  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery  
029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB In human heart, we detected mRNAs and proteins for C1q, C1r, C1s, C2, C3, C4, C5, C6, C7, C8, and C9 with the use of reverse transcriptase- polymerase chain reaction, Western blotting, and immunohistochemical techniques. We found an upregulation of both mRNAs and proteins in areas of recent and old myocardial infarctions. In both situations, the classical complement pathway was activated, with C4d, C3d, and the membrane attack complex (C5b-9) being deposited on damaged cardiac myocytes. These activated complement components were also identified on Western blots of infarcted tissue. Complement mRNAs in infarcted heart tissue were higher than those in liver, and liver complement mRNAs were not upregulated in cases with infarcted hearts. Our results establish that (1) complement proteins are endogenously produced by human heart; (2) the classical complement pathway is fully activated after myocardial infarction; (3) complement activation is directly involved in myocardial damage after ischemic insults; and (4) damage from complement activation may be chronically sustained. These data suggest that inhibition of the complement system should be effective in treating myocardial infarction.

L35 ANSWER 43 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 1998315398 EMBASE  
TITLE: Synthesis, solution conformation and interleukin-6-related activities of interleukin-6 peptides.  
AUTHOR: Bosze S.; Kajtar J.; Szabo R.; Falus A.; Hudecz F.  
CORPORATE SOURCE: Dr. F. Hudecz, Research Group of Peptide Chemistry, Hungarian Academy of Sciences, Eotvos Lorand University, POB 32, Budapest 112, H-1518, Hungary.  
fhudecz@ludens.elte.hu  
SOURCE: Journal of Peptide Research, (1998) 52/3 (216-228).  
Refs: 63  
ISSN: 1397-002X CODEN: JPERFA  
COUNTRY: Denmark  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 026 Immunology, Serology and Transplantation  
029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Interleukin-6 (IL-6) is a member of the cytokine superfamily characterised by a wide variety of biological activities on various cell types. IL-6 exerts pleiotropic activities on hematopoiesis in the immune response and it is the main regulator of acute-phase protein synthesis in liver cells.



According to structure-function studies, residues of helix A located at the N-terminal part and/or helix D of the C-terminal part of the protein are involved in the induction of acute-phase responses. Two groups of synthetic peptides corresponding to the 18-46 N-terminal and the 168-185 C-terminal regions of the IL-6 were prepared by solid-phase synthesis to identify structural requirements for induction of fibrinogen or complement factor B synthesis. These peptides were characterised by amino acid analysis, analytical reversed-phase high-performance liquid chromatography, fast atom bombardment **mass spectrometry**, and circular dichroism (CD) spectroscopy. CD results showed that under appropriate conditions both 18-46 and 168-185 related peptides are able to adopt markedly ordered conformation. We demonstrated that even octapeptides from the N-terminal part and truncated derivatives of the C-terminal region preserved some tendency to display the CD curve of periodic conformation. The ability of the peptides to induce de novo synthesis of acute-phase proteins was evaluated by **measuring** fibrinogen and complement factor B levels in the supernatants of human HepG2 cells. These results showed that residues 21-34 are critical for eliciting fibrinogen synthesis in the presence or absence of IL-6. In contrast, the full-length 168-185 peptide is required for the induction of complement factor B response.

L35 ANSWER 44 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1998124953 EMBASE

TITLE: Evaluation of biocompatibility of heparin-coated circuits.

AUTHOR: Murakami A.; Aiba M.; Murata N.; Yamada M.; Michihata T.; Inoue K.; Takaba T.

CORPORATE SOURCE: A. Murakami, Dept. of First Surgery of Medicine, Showa University, 1-5-8 Hatanodai Shinagawa-ku, Tokyo, Japan

SOURCE: Japanese Journal of Artificial Organs, (1998) 27/1 (113-117).

Refs: 15

ISSN: 0300-0818 CODEN: JNZKA7

COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 009 Surgery  
027 Biophysics, Bioengineering and Medical Instrumentation  
037 Drug Literature Index

LANGUAGE: Japanese

SUMMARY LANGUAGE: English; Japanese

AB To assess the biocompatibility of heparin-coated cardiopulmonary circuits using Capiox SX, filters and tubing sets (TERUMO. CO.), we had **measured** as follows in group H (using heparin-coated circuits, n=9) and in group C (using ordinary circuits, control group, n=9). Compliments (C3a, C4a), granuloocyte elastase (GEL), cytokines (Interleukin 6 and 8), Tumor Necrosis factor (TNF), thrombin-antithrombin III complex (TAT), fibrinopeptide A (FPA), fibrinogen, antithrombin-III (AT-III), D-dimer, .alpha. 2- PI, renal function, liver function were **measured** before, during and immediately after **cardio**-pulmonary bypass (CPB), 24 hours after CPB (24H), and on the third operative day (3D). No statistically significant changes were found in all factors between the two groups. But peak levels of IL-6, C3a and GEL at AF in group H were lower than in group C. Furthermore, D- dimer reached its maximum value at AF in group C, but at 24H in group H. This study demonstrates the tendency that the use of heparin-coated circuits reduce the release of IL-6, C3a, GEL and D-dimer, but the method of evaluation of organ damages should be reconsidered.

L35 ANSWER 45 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:674436 HCAPLUS

DOCUMENT NUMBER: 127:330102

TITLE: Combination of decay-accelerating factor expression and .alpha.1,3-galactosyltransferase knockout affords added protection from human complement-mediated injury

AUTHOR(S): Van Denderen, Bryce J. W.; Salvaris, Evelyn; Romanella, Margarita; Aminian, Atousa; Katerelos, Marina; Tange, Margaret J.; Pearse, Martin J.; D'apice, Anthony J. F.

CORPORATE SOURCE: Immunology Research Centre, St. Vincent's Hospital, Fitzroy, 3065, Australia

SOURCE: Transplantation (1997), 64(6), 882-888

CODEN: TRPLAU; ISSN: 0041-1337

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hyperacute rejection (HAR) currently prevents the use of pigs as organ donors for humans. It is now generally accepted that the key instigators of HAR are naturally occurring xenoantibodies against the terminal disaccharide galactose .alpha.1,3-galactose (Gal), and the species incompatibility between human complement and porcine complement regulatory mols. Using two in vitro models and an ex vivo mouse heart perfusion model, the authors have shown previously that cells and tissues from Gal knockout (Gal KO) and transgenic mice expressing the human cell surface complement regulator decay-accelerating factor (DAF/CD55) are partially, but not completely, protected from human complement-mediated injury. In the present study, Gal KO mice were crossed with DAF transgenic mice and bred to homozygosity (DAF/Gal KO). Isolated splenocytes were incubated with human serum, and the protective effect of DAF and Gal KO was assessed by measuring complement deposition and cell lysis. Hearts perfused ex vivo with human plasma were examd. for human antibody and complement deposition, and assessed functionally by **measuring** work performed by the **heart**. Splenocytes from DAF/Gal KO mice were found to be more resistant to complement-mediated injury than cells from either DAF transgenic or Gal KO mice. In addn., hearts from DAF/Gal KO mice, when perfused with human plasma, displayed prolonged survival compared with hearts from Gal KO mice. This was assocd. with a redn. in the extent of endothelial deposition of IgG, IgM, and **complement C3b**. These findings demonstrate that expression of human DAF in assocn. with elimination of the Gal epitope provides added protection from complement-mediated injury in these models of HAR.

L35 ANSWER 46 OF 87 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1997:362827 BIOSIS

DOCUMENT NUMBER: PREV199799654760

TITLE: Clinical evaluation of the centrifugal pump in open heart surgery: A comparative study of different pumps.

AUTHOR(S): Takarabe, Kyoumi (1); Yoshikai, Masaru; Murayama, Junichi; Hamada, Masakatsu; Ito, Tsuyoshi

CORPORATE SOURCE: (1) Koga Hosp., 106-1 Tenjin-cho, Kurume City, Fukuoka 830 Japan

SOURCE: Artificial Organs, (1997) Vol. 21, No. 7, pp. 760-762.

ISSN: 0160-564X.

DOCUMENT TYPE: Article

LANGUAGE: English

AB The centrifugal pump is now widely used in open heart surgery for its clinical benefits related to the blood elements and the coagulation system. The purpose of this study was to compare the clinical performances

of and the outcomes offered by 4 types of centrifugal pumps. For each pump, we investigated the effects on the blood elements, coagulation system, complements, and immunoglobulins during open heart surgery. Four types of centrifugal pumps were used: the HPM-15 (Nikkiso Co.), the Capiox (Terumo Co.), the Lifestream (St. Jude Medical Co.), and the BP-80 (Medtronic, BioMedicus Co.). The platelet count, lactate dehydrogenase (LDH), antithrombin III (AT III), thrombin-antithrombin complex (TAT), complements (C3, C4, and CH-50), and immunoglobulins (IgG, IgA, and IgM) were **measured** before and after **cardiopulmonary** bypass (CPB). The platelet count was decreased more significantly by the HPM-15 than by any of the other pumps. The other parameters showed no difference among the 4 pumps. In clinical use, each of the 4 types of centrifugal pumps was safe.

L35 ANSWER 47 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:433142 HCAPLUS

DOCUMENT NUMBER: 125:108203

TITLE: Disulfide bond structure determination and biochemical analysis of glycoprotein C from herpes simplex virus

AUTHOR(S): Rux, Ann H.; Moore, William T.; Lambris, John D.; Abrams, William R.; Peng, Charline; Friedman, Harvey M.; Cohen, Gary H.; Eisenberg, Roselyn J.

CORPORATE SOURCE: Dep. Microbiology, Univ. Pennsylvania, Philadelphia, PA, 19104, USA

SOURCE: Journal of Virology (1996), 70(8), 5455-5465

CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A biochem. anal. of glycoprotein C (gC) of herpes simplex virus was undertaken to further characterize the structure of the glycoprotein and to det. its disulfide bond arrangement. We used three recombinant forms of gC, gC1(457t), gC1(.DELTA.33-123t), and gC2(426t), each truncated prior to the transmembrane region. The proteins were expressed and secreted by using a baculovirus expression system and have been shown to bind to monoclonal antibodies which recognize discontinuous epitopes and to **complement** component **C3b** in a dose-dependent manner. We confirmed the N-terminal residues of each mature protein by Edman degrdn. and confirmed the internal deletion in gC1(.DELTA.33-123t). The mol. wt. and extent of glycosylation of gC1(457t), gC1(.DELTA.33-123t), and gC2(426t) were detd. by treating each protein with endoglycosidases and then subjecting it to sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and **mass spectrometric** anal. The data indicate that eight to nine of the predicted N-linked oligosaccharide sites on gC1(457t) are occupied by glycans of approx. 1,000 Da. In addn., O-linked oligosaccharides are present on gC1(457t), primarily localized to the N-terminal region (amino acids [aa] 33 to 123) of the protein. The gC2(426t) contains N-linked oligosaccharides, but no O-linked oligosaccharides were detected. To det. the disulfide bond arrangement of the eight cysteines of gC1(457t), the protein was cleaved with cyanogen bromide. SDS-PAGE anal. followed by Edman degrdn. identified three cysteine-contg. fragments which are not connected by disulfide linkages. Chem. modification of cysteines combined with matrix-assisted **laser desorption** ionization **mass spectrometry** identified disulfide bonds between cysteine 1 (aa 127) and cysteine 2 (aa 144) and between cysteine 3 (aa 286) and cysteine 4 (aa 347). Further proteolysis of the cyanogen bromide-generated fragment contg. cysteine 5 through cysteine 8, combined with **mass spectrometry** and Edman degrdn., showed that

disulfide bonds link cysteine 5 (aa 386) to cysteine 8 (aa 442) and cysteine 6 (aa 390) to cysteine 7 (aa 419). A similar disulfide bond arrangement is postulated to exist in gC homologs from other herpesviruses.

L35 ANSWER 48 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 21  
 ACCESSION NUMBER: 1997:105823 HCAPLUS  
 DOCUMENT NUMBER: 126:195034  
 TITLE: Effect of sodium nitroprusside on complement activation induced by cardiopulmonary bypass: A clinical and experimental study  
 AUTHOR(S): Seghaye, Marie-Christine; Duchateau, Jean; Grabitz, Ralph G.; Wolff, Thibault; Marcus, Christiane; Engelhardt, Wolfgang; Hornchen, Helmut; Messmer, Bruno J.; von Bernuth, Goetz  
 CORPORATE SOURCE: Department of Pediatric Cardiology, RWTH Aachen, Aachen, D-52057, Germany  
 SOURCE: Journal of Thoracic and Cardiovascular Surgery (1996), 111(4), 882-892  
 CODEN: JTCSAQ; ISSN: 0022-5223  
 PUBLISHER: Mosby-Year Book  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Complement activation and leukocyte stimulation were prospectively studied during and after cardiopulmonary bypass in 16 children receiving sodium nitroprusside - a nitrovasodilator releasing nitric oxide - for vasodilation during the cooling and rewarming periods of extracorporeal circulation. Results were compared with those in 29 patients who were not treated with sodium nitroprusside during the operation. Patients treated with sodium nitroprusside had significantly less C3 conversion during **cardiopulmonary** bypass as **measured** by the ratio C3d/C3 ( $p < 0.05$ ) and significantly less C5a liberation immediately after cardiopulmonary bypass ( $p < 0.005$ ) than patients not treated with sodium nitroprusside. C4 was not overtly consumed in our series. Leukocyte count during the rewarming period of cardiopulmonary bypass, but not leukocyte elastase release during cardiopulmonary bypass, was significantly reduced in patients treated with sodium nitroprusside ( $p < 0.05$ ). In vitro expts. were conducted to analyze the effect of sodium nitroprusside on complement hemolytic activity initiated by the classic and the alternate pathways and on zymosan-induced C3 conversion by the activation of the alternate pathway. The in vitro expts. clearly demonstrate inhibition of complement hemolytic activity by sodium nitroprusside in the sera tested. The 50% inhibitory concn. of sodium nitroprusside on the available complement hemolytic activity was less through the alternate pathway than through the classic one ( $4.2 \pm 0.8$  mmol/L and  $14.0 \pm 2.88$  mmol/L, resp.). The decrease of complement hemolytic activity **measured** was dose-dependent and was enhanced by the sodium nitroprusside preincubation of the sera tested. This effect was related to the duration of preincubation. Sodium nitroprusside photodegradn. (enhancing nitric oxide release) increased the anticomplementary effect of the drug, reducing the 50% inhibitory concn. on complement hemolytic activity to 0.24 to 0.02 mmol/L for the alternate pathway and  $2.74 \pm 0.3$  mmol/L for the classic pathway. The zymosan-induced C3 conversion was inhibited by sodium nitroprusside. Nitroglycerin and isosorbide dinitrate (other nitric oxide donors) had in vitro effects on complement hemolytic activity similar to those of nonphotodegraded sodium nitroprusside at similar concns. (1 mmol/L). Our results suggest that sodium nitroprusside, both in vitro and in vivo, has an inhibiting effect on complement activation initiated by both classic

and alternate pathways and that this effect is mediated by nitric oxide release from sodium nitroprusside. This is the first report on the anticomplementary effect of sodium nitroprusside by nitric oxide release.

L35 ANSWER 49 OF 87 MEDLINE DUPLICATE 22  
 ACCESSION NUMBER: 96393370 MEDLINE  
 DOCUMENT NUMBER: 96393370 PubMed ID: 8800157  
 TITLE: Inflammatory reaction and capillary leak syndrome related to cardiopulmonary bypass in neonates undergoing cardiac operations.  
 AUTHOR: Seghaye M C; Grabitz R G; Duchateau J; Busse S; Dabritz S; Koch D; Alzen G; Hornchen H; Messmer B J; Von Bernuth G  
 CORPORATE SOURCE: Department of Pediatric Cardiology, Aachen University of Technology, Germany.  
 SOURCE: JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY, (1996 Sep) 112 (3) 687-97.  
 Journal code: 0376343. ISSN: 0022-5223.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 ENTRY MONTH: 199610  
 ENTRY DATE: Entered STN: 19961106  
 Last Updated on STN: 19961106  
 Entered Medline: 19961022

AB We studied the inflammatory reaction related to cardiopulmonary bypass in 24 neonates (median age 6 days) undergoing the arterial switch operation for simple transposition of the great arteries, with respect to the development of postoperative capillary leak syndrome. Complement proteins, leukocyte count, tumor necrosis factor-alpha, and histamine levels were determined before, during, and after cardiopulmonary bypass. Additionally, protein movement from the intravascular into the extravascular space during **cardiopulmonary** bypass was assessed by the **measurement** of plasma concentrations of proteins with molecular weights ranging from 21,200 to 718,000. Capillary leak syndrome developed in 13 of the 24 neonates. Patients with capillary leak syndrome, as compared with those without, had preoperatively higher C5a levels (C5a, 3.0 +/- 0.6 microgram/L vs 0.9 +/- 0.2 microgram/L) (mean +/- standard error of the mean) ( $p < 0.05$ ) and higher leukocyte counts (leukocytes, 17.9 +/- 2.1 X 10(3) cells/ml versus 11.7 +/- 0.8 X 10(3) cells/ml) ( $p < 0.05$ ), suggesting in these neonates a preoperative inflammatory state. Preoperative clinical and operative data were identical in both patient groups. Before cardiopulmonary bypass, serum protein concentrations were similar in all patients. Ten minutes after institution of cardiopulmonary bypass, protein concentrations fell to significantly lower values in patients with capillary leak syndrome than in those without: albumin (19% +/- 1.5% vs 30% +/- 6% of the prebypass value,  $p < 0.05$ ), immunoglobulin G (17% +/- 1.5% vs 29% +/- 5.5%,  $p < 0.001$ ), and alpha 2-macroglobulin (15% +/- 1.2% vs 25% +/- 4%,  $p < 0.02$ ). During cardiopulmonary bypass, albumin concentrations remained significantly lower in patients with capillary leak syndrome than in those without, whereas hematocrit values were similar in both groups. During cardiopulmonary bypass, patients with capillary leak syndrome also had lower concentrations of **complement** proteins C3 and C4 but not C1 inhibitor. C3d/C3 ratio and C5a levels were similar in both patient groups. In contrast, histamine liberation during cardiopulmonary bypass was significantly more pronounced in patients with capillary leak syndrome than in those without (725.2 +/- 396.7 pg/ml vs -54.1 +/- 58.4 pg/ml,  $p < 0.05$ ). Tumor necrosis factor-alpha levels after protamine administration

were also significantly higher in patients with capillary leak syndrome (38.1 +/- 10.0 pg/ml vs 15.3 +/- 3.4 pg/ml,  $p < 0.05$ ). Leukocyte count during and after cardiopulmonary bypass was similar in both patient groups. This study demonstrates increased protein leakage as early as 10 minutes after initiation of.

L35 ANSWER 50 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96255758 EMBASE

DOCUMENT NUMBER: 1996255758

TITLE: Key role of the alternate complement pathway in hyperacute rejection of rat hearts transplanted into fetal sheep.

AUTHOR: Rajasinghe H.A.; Reddy V.M.; Hancock W.W.; Sayegh M.H.; Hanley F.L.

CORPORATE SOURCE: Division of Cardiothoracic Surgery, University of California, 505 Parnassus Avenue, San Francisco, CA 94143, United States

SOURCE: Transplantation, (1996) 62/3 (407-411).

ISSN: 0041-1337 CODEN: TRPLAU

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
018 Cardiovascular Diseases and Cardiovascular Surgery  
026 Immunology, Serology and Transplantation

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Hyperacute rejection (HAR) mediated by xenoreactive natural antibodies (XNA), which are thought to develop in early infancy, is a major impediment to transplantation between widely disparate species. The ability to **diagnose** certain forms of congenital **heart** defects early in prenatal life suggests the potential for these defects to be corrected by cardiac transplantation, prior to the development of XNA and host immunocompetence. This study investigated whether discordant cardiac xenotransplantation into fetal and neonatal recipients might obviate HAR due to the relative lack of XNA. Six neonatal lambs at 3 days (n=3) or 7 days (n=3) of life, and two fetal lambs at 125 and 142 days of gestation (term = 145 days) received cardiac grafts from adult Wistar-Furth (275-350 g) rats. All eight cardiac xenografts showed clinical evidence of HAR, with rapid swelling, loss of contractility, and ecchymosis and a mean survival time of 12.5 +/- 6.4 min. Sections of explanted grafts showed classical histologic features of HAR, including interstitial hemorrhages, platelet microthrombi, and edema, without leukocyte infiltration. Immunopathology of grafts harvested from fetal recipients showed a lack of significant intragraft deposition of sheep IgM, IgG, or C1q, but widespread endothelial labeling for C3, factor B, and properdin. In contrast, grafts in neonatal recipients showed IgM, IgG, and C1q deposition, as well as C3, factor B, properdin, and terminal complement (C) components. Fibrin deposition and platelet thrombi were seen in both groups of recipients. Injection of cobra venom factor resulted in prolongation of cardiac xenograft survival in neonatal lambs (n=3) to 12 hr. Analysis by immunohistology showed that normal sera from neonatal and adult, but not fetal, sheep contained IgM and IgG XNA reactive with rat cells. In conclusion, rodent grafts transplanted into fetal sheep undergo HAR, likely through direct activation of the alternate pathway of C, whereas neonatal lambs acquire XNA in the very early postnatal period and reject rat hearts through activation of both the classical and alternate pathways of C. Thus, at least in some species combinations, cardiac transplantation during the early postnatal period, or even in utero, may still be subject to development of HAR.

L35 ANSWER 51 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:555068 HCAPLUS

DOCUMENT NUMBER: 125:269545

TITLE: **Mass spectrometric** analyses of the activation products of the third component of complement

AUTHOR(S): Moore, william T.; Lambris, John D.

CORPORATE SOURCE: Department Pathology and Laboratory Medicine, University Pennsylvania, Philadelphia, PA, 19104, USA

SOURCE: Techniques in Protein Chemistry VII, [Symposium of the Protein Society], 9th, Boston, July 8-12, 1995 (1996), Meeting Date 1995, 81-91. Editor(s): Marshak, Daniel R. Academic: San Diego, Calif.

CODEN: 63GTAE

DOCUMENT TYPE: Conference

LANGUAGE: English

AB **Mass spectrometry** was used to explore the structures comprising the functional life-cycle of C3 at the protein level. The goal was to fully characterize the C3 mol. and its fragments at the protein level cataloging any post-translational covalent modifications. The initial results indicated that the **mass spectrometric** approach is also yielding information about the conformational changes that exist in this family of protein derivs.

L35 ANSWER 52 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96014881 EMBASE

DOCUMENT NUMBER: 1996014881

TITLE: In vitro and in vivo inhibition of complement activity by a single-chain Fv fragment recognizing human C5.

AUTHOR: Evans M.J.; Rollins S.A.; Wolff D.W.; Rother R.P.; Norin A.J.; Therrien D.M.; Grijalva G.A.; Mueller J.P.; Nye S.H.; Squinto S.P.; Wilkins J.A.

CORPORATE SOURCE: Department of Molecular Development, Alexion Pharmaceuticals, 25 Science Park, New Haven, CT 06511, United States

SOURCE: Molecular Immunology, (1995) 32/16 (1183-1195).

ISSN: 0161-5890 CODEN: IMCHAZ

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery  
026 Immunology, Serology and Transplantation  
029 Clinical Biochemistry  
030 Pharmacology  
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Complement activation has been implicated in the pathogenesis of several human diseases. Recently, a monoclonal antibody (N19-8) that recognizes the human complement protein C5 has been shown to effectively block the cleavage of C5 into C5a and C5b, thereby blocking terminal complement activation. In this study, a recombinant N19-8 scFv antibody fragment was constructed from the N19-8 variable regions, and produced in both mammalian and bacterial cells. The N19-8 scFv bound human C5 and was as potent as the N19-8 monoclonal antibody at inhibiting human C5b-9-mediated hemolysis of chicken erythrocytes. In contrast, the N19-8 scFv only partially retained the ability of the N19-8 monoclonal antibody to inhibit C5a generation. To investigate the ability of the N19-8 scFv to inhibit complement-mediated tissue damage, complement-dependent myocardial injury was induced in isolated mouse hearts by perfusion with Krebs-Henseleit

buffer containing 6% human plasma. The perfused hearts sustained extensive deposition of human C3 and C5b-9, resulting in increased coronary artery perfusion pressure, end-diastolic pressure, and a decrease in heart rate until the hearts ceased beating approximately 10 min after the addition of plasma. Hearts treated with human plasma supplemented with either the N19-8 monoclonal antibody or the N19-8 scFv did not show any **detectable** changes in **cardiac** performance for at least 1 hr following the addition of plasma. Hearts treated with human plasma alone showed extensive deposition of C3 and C5b-9, while hearts treated with human plasma containing the N19-8 scFv showed extensive deposition of C3, but no **detectable** deposition of C5b-9. Administration of a 100 mg bolus dose of N19-8 scFv to rhesus monkeys inhibited the serum hemolytic activity by at least 50% for up to 2 hr. Pharmacokinetic analysis of N19-8 scFv serum levels suggested a two-compartment model with a  $T(1/2)_{\alpha}$  of 27 min. Together, these data suggest the recombinant N19-8 scFv is a potent inhibitor of the terminal complement cascade and may have potential in vivo applications where short duration inhibition of terminal complement activity is desirable.

L35 ANSWER 53 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 94144842 EMBASE

DOCUMENT NUMBER: 1994144842

TITLE: **Detection** of rat antibodies against hamster **heart**: Reactivity of natural antibodies in a concordant model.

AUTHOR: Lillevang S.T.; Steinbruchel D.A.; Kemp E.

CORPORATE SOURCE: Department of Clinical Immunology, Odense University Hospital, DK-5000 Odense C, Denmark

SOURCE: Transplantation Proceedings, (1994) 26/2 (989-991).

ISSN: 0041-1345 CODEN: TRPPA8

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 009 Surgery

026 Immunology, Serology and Transplantation

LANGUAGE: English

L35 ANSWER 54 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 94026125 EMBASE

DOCUMENT NUMBER: 1994026125

TITLE: Purification and characterization of a collagen-degrading protease from *Porphyromonas gingivalis*.

AUTHOR: Bedi G.S.; Williams T.

CORPORATE SOURCE: Biological Research, Magainin Pharmaceuticals Inc., 5110 Campus Dr., Plymouth Meeting, PA 19462, United States

SOURCE: Journal of Biological Chemistry, (1994) 269/1 (599-606).

ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A trypsin-like protease was purified from spent culture medium of oral pathogen *Porphyromonas gingivalis* by chromatography on columns of DEAE-Sephadex, gel filtration on Sephadex G-100, and chromatofocusing on PBE-94. Purified enzyme showed a single band on SDS-polyacrylamide gel electrophoresis with an estimated molecular weight of 55,000. Purified protease hydrolyzed type I, III, IV, and V collagen from human placenta, and type I collagen from rat tail and calf skin, but did not hydrolyze type II collagen from chicken sternal cartilage. The purified enzyme also



hydrolyzed the C3 component of complement, fibrinogen, fibronectin, .alpha.1-antitrypsin, .alpha.2-macroglobulin, apotransferrin, and human serum albumin. The hydrolytic activity of the purified enzyme on chromogenic substrates was limited to substrates with arginine in the P-1 position, although synthetic peptides were also cleaved at Lys-X linkage. The enzyme was activated by reducing agents dithiothreitol, L-cysteine, and glutathione and inhibited by cysteine protease inhibitors N-ethylmaleimide, iodoacetic acid, and iodoacetamide. The enzyme was also inhibited by trans-epoxysuccinyl-L-leucylamido(4- guanidino)butane (E-64), leupeptin, antipain, salivary histidine-rich protein (HRP-5), soybean trypsin inhibitor, and EDTA. Since the protease is able to degrade the connective tissue components of periodontal tissue as well as components of host defense mechanism, this enzyme may be a potent virulence factor of *P. gingivalis* involved in invasion and tissue destruction.

L35 ANSWER 55 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 94072592 EMBASE  
 DOCUMENT NUMBER: 1994072592  
 TITLE: Neutrophil lactoferrin release during open heart surgery is unrelated to complement activation.  
 AUTHOR: Shastri K.A.; Logue G.L.; Stern M.P.; Raza S.; O'Connor B.M.; Bovill J.J.; Hoover E.L.  
 CORPORATE SOURCE: Hematology Division, Veterans Affairs Medical Center, 3495 Bailey Ave., Buffalo, NY 14215, United States  
 SOURCE: ASAIO Journal, (1994) 40/1 (56-61).  
 ISSN: 1058-2916 CODEN: AJOUET  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 009 Surgery  
 018 Cardiovascular Diseases and Cardiovascular Surgery  
 026 Immunology, Serology and Transplantation  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB The relationship between neutrophil activation and complement activation during open heart surgery was evaluated by measuring plasma lactoferrin and C3a des Arg (C3a) in 30 adult patients undergoing coronary artery surgery. Measurements were made before induction of anesthesia, before cardiopulmonary bypass, at the end of bypass, and 10 min after protamine infusion. Changes in the measured parameters thus reflected activation during the three distinct phases of cardiac surgery: pre cardiopulmonary bypass, the bypass phase, and the heparin neutralization phase. A major rise in lactoferrin occurred in the pre bypass period, from 99 .+-. 13 (mean .+-. SEM) to 647 .+-. 48 ng/ml ( $p < 0.001$ ). During this time, C3a levels did not rise significantly (384 .+-. 22 to 439 .+-. 36 ng/ml). The bypass procedure resulted in a rise of both lactoferrin and C3a levels, with lactoferrin reaching 1,092 .+-. 69 ng/ml and C3a increasing to 1,884 .+-. 179 ng/ml after bypass ( $p < 0.001$  for both). In individual patients, however, the changes in lactoferrin during bypass did not correlate with changes in C3a levels ( $r = -0.06$ ). After protamine infusion, C3a levels reached 3,301 .+-. 324 ng/ml, while the plasma lactoferrin levels declined to 522 .+-. 57 ng/ml. Thus, during open heart surgery, neutrophil activation, as measured by plasma lactoferrin concentration, does not correlate with complement activation resulting from the bypass procedure or the protamine neutralization of heparin. The potential clinical relevance of the neutrophil granular release of lactoferrin is discussed.

L35 ANSWER 56 OF 87 MEDLINE  
 ACCESSION NUMBER: 94164610 MEDLINE

DOCUMENT NUMBER: 94164610 PubMed ID: 8119656  
TITLE: Analysis of cardiac function of discordant heart xenografts using a blood-perfused, isolated, supported heart model.  
AUTHOR: Miyatake T  
CORPORATE SOURCE: Second Department of Surgery, Hokkaido University School of Medicine, Sapporo, Japan.  
SOURCE: HOKKAIDO IGAKU ZASSHI. HOKKAIDO JOURNAL OF MEDICAL SCIENCE, (1994 Jan) 69 (1) 35-45.  
Journal code: 17410290R. ISSN: 0367-6102.  
PUB. COUNTRY: Japan  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: Japanese  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199404  
ENTRY DATE: Entered STN: 19940412  
Last Updated on STN: 19960129  
Entered Medline: 19940404

AB Changes in cardiac function during hyperacute rejection are not fully understood because of lack of appropriate models. In this study, a blood-perfused, isolated, supported heart model was employed for the analysis of cardiac function in discordant heart xenografts. Methods: Experiment 1: Changes in left ventricular end-systolic pressure (LVESP) and coronary perfusion pressure (CPP) were **measured** for 120 min. Dry heart weight after perfusion was **measured** in the following 4 groups: group A; isolated rat heart perfused with blood from support rat, group B; guinea pig heart, support guinea pig, group C; guinea pig heart, support rat, and group D; guinea pig heart, support rat with cobra venom factor (CVF) pretreatment. **Complement C3** of support rat serum in group C and group D was **measured** by single radial immunodiffusion (SRID). Experiment 2: Fifteen guinea pig hearts perfused with blood from untreated support rats were analyzed for correlation between survival time and LVESP, and CPP as well. Results: In groups A and B, LVESP and CPP was stable up to 120 min. In group C, 4 out of 6 hearts were stopped beating within 120 min. The difference between LVESP at 10 min in group C and that in group B was not obtained, possibly due to high variation of values in group C, whereas CPP in group C was higher than that in group B ( $p < 0.05$ ). In group D, CVF was shown to deplete **complement C3**. Group D showed constant LVESP and CPP, similar to non-xenograft groups. Dry heart weight of group C was larger than those of group B and D. There were positive correlations between survival time and LVESP at 10 min, and increasing rate of LVESP after 10 min as well. A negative correlation between survival time and CPP at 10 min was observed, while no correlation was obtained between survival time and increasing rate of CPP after 10 min. Conclusions: 1) Decreases in LVESP and increases in CPP in xenograft group are considered to be due to hyperacute rejection. 2) These changes can be abolished by depletion of C3. 3) Guinea pig hearts can work well in xenograft condition as in allograft condition in certain circumstances, i.e. depletion of C3. 4) The blood-perfused, isolated, supported heart model is useful for the analysis of cardiac function in discordant xenografts.

L35 ANSWER 57 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 94228980 EMBASE  
DOCUMENT NUMBER: 1994228980  
TITLE: Complement, leukocytes, and leukocyte elastase in full-term neonates undergoing cardiac operation.  
AUTHOR: Seghaye M.-C.; Duchateau J.; Grabitz R.G.; Nitsch G.; Marcus C.; Messmer B.J.; Von Bernuth G.

CORPORATE SOURCE: Department of Pediatric Cardiology, RWTH Aachen, 52057  
Aachen, Germany  
SOURCE: Journal of Thoracic and Cardiovascular Surgery, (1994)  
108/1 (29-36).  
ISSN: 0022-5223 CODEN: JTCSAQ  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery  
018 Cardiovascular Diseases and Cardiovascular Surgery  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB In 13 neonates undergoing cardiac operations for congenital cardiac defects, complement, leukocytes, and leukocyte elastase were studied during and after cardiopulmonary bypass. All but two neonates received prostaglandin E1 before the operation. The C3d/C3 ratio rose significantly during cardiopulmonary bypass from 0.86  $\pm$  0.55 to 1.40  $\pm$  0.56 (mean  $\pm$  standard deviation;  $p < 0.0001$ ). Abnormally elevated C5a levels (18.6  $\pm$  7.3  $\mu$ g/L) were **measured** at the end of **cardiopulmonary** bypass. C4 was not overtly consumed during the procedure. Leukocytes fell from a preoperative value of 10.06  $\pm$  3.15  $\times 10^9$ /L to 3.21  $\pm$  0.64  $\times 10^9$ /L after beginning of cardiopulmonary bypass ( $p < 0.0001$ ) and rose at the end of the procedure from 2.33  $\pm$  0.67  $\times 10^9$ /L to 7.19  $\pm$  1.84  $\times 10^9$ /L, after protamine administration ( $p < 0.0001$ ). Neutrophils fell from a preoperative value of 5.14  $\pm$  1.18  $\times 10^9$ /L to 1.46  $\pm$  0.35  $\times 10^9$ /L after beginning of cardiopulmonary bypass and rose at the end of extracorporeal circulation from 1.00  $\pm$  0.31  $\times 10^9$ /L to 4.10  $\pm$  1.18  $\times 10^9$ /L, after protamine administration ( $p < 0.005$ ). Elastase release occurred in all neonates during cardiopulmonary bypass and averaged 331.5  $\pm$  175.7  $\mu$ g/L. Complement activation and leukocyte stimulation did not correlate with postoperative complications or outcome. This study demonstrates complement activation and leukocyte stimulation in neonates undergoing cardiac operation.

L35 ANSWER 58 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:668581 HCAPLUS  
DOCUMENT NUMBER: 119:268581  
TITLE: The adipsin-acylation stimulating protein system and regulation of intracellular triglyceride synthesis  
AUTHOR(S): Baldo, Allain; Sniderman, Allan D.; St-Luce, Serena; Avramoglu, Rita Kohen; Hoang Bich, Magdalena Maslowska; Maslowska, Magdalena; Monge, Juan Carlos; Bell, Alex; Mulay, Shree; Cianflone, Katherine  
CORPORATE SOURCE: McGill Unit Prev. Cardiovasc. Dis., R. Victoria Hosp., Montreal, QC, H3A 1A1, Can.  
SOURCE: Journal of Clinical Investigation (1993), 92(3), 1543-7  
CODEN: JCINAO; ISSN: 0021-9738  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The authors have previously characterized an activity from human plasma that markedly stimulates triglyceride synthesis in cultured human skin fibroblasts and human adipocytes. Based on its in vitro activity the authors named the active component acylation stimulating protein (ASP). The mol. identity of the active serum component has now been detd. N-terminal sequence anal., ion spray ionization **mass spectroscopy**, and amino acid compn. anal. all indicate that the active purified protein is a fragment of the third component of plasma **complement**, C3a-des-Arg. As well, reconstitution expts. with complement factors B, D, and **complement C3**, the

components necessary to generate C3a, have confirmed the identity of ASP as C3a. ASP appears to be the final effector mol. generated by a novel regulatory system that modulates the rate of triglyceride synthesis in adipocytes.

L35 ANSWER 59 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 23  
 ACCESSION NUMBER: 1994:214123 HCAPLUS  
 DOCUMENT NUMBER: 120:214123  
 TITLE: Changes in cardiorespiratory dynamics and plasma chemical mediators after total thoracic esophagectomy in dogs with endotoxemia  
 AUTHOR(S): Nishida, Hiroshi  
 CORPORATE SOURCE: Sch. Med., Kurume Univ., Kurume, 830, Japan  
 SOURCE: Kurume Igakkai Zasshi (1993), 56(11), 1094-106  
 CODEN: KIZAAL; ISSN: 0368-5810  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Japanese

AB Anesthetized mongrel dogs were divided in to 6 groups as follows. Group A (control model: surgery alone) underwent total thoracic esophagectomy. Group B (control model; endotoxemia) underwent i.v. administration of lipopolysaccharide. Group C (endotoxin shock model following surgery) also underwent the same protocol as for group A with group B. Group D, E, and F, who underwent the same protocol as group C, followed by postoperative i.v. continuous infusion of thromboxane A2 (TXA2) synthetase inhibitor OKY-046, leukotriene antagonist ONO-RS-411, and superoxide dismutase, resp. Changes in cardiorespiratory function in each model were monitored by **measuring cardiac** output (CO), blood pressure (BP), pulmonary arterial pressure (PAP), pulmonary wedge pressure (PWP), extravascular lung water (EVLW), blood gas, lung resistance and dynamic lung compliance at pre-treatment and 1, 3, 6, 12 h after resp. treatment. Models in group C showed a severe cardiorespiratory failure immediately after surgery and they were dying at the 12th postoperative h. In these models, cardiac output decreased more than 60% in comparison with preoperative values, plasma concn. of TXB2 significantly increased including mild to moderate increase in leukotrienes and .alpha.2-plasmin inhibitor-plasmin complex (.alpha.2-PI.cntdot.PM). Cardiorespiratory functions in group D, E, and F were well preserved until the end of this investigation and the rise in plasma concns. of TXB2 and .alpha.2-PI.cntdot.PM were significantly suppressed using resp. pharmacotherapy. Within the 3 groups, OKY-046 administration showed max. inhibition of TXA2 synthetase accompanied by a well preserved cardiorespiratory function with no significant differences. Thus, OKY-046 administration is the most effective pharmacotherapy as an initial counter **measure** for endotoxemia following esophageal surgery, owing its strong counter action against vasoconstriction and bronchospasm.

L35 ANSWER 60 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 94015676 EMBASE  
 DOCUMENT NUMBER: 1994015676  
 TITLE: Complement activation during cardiopulmonary bypass in infants and children: Relation to postoperative multiple system organ failure.  
 AUTHOR: Seghaye M.C.; Duchateau J.; Grabitz R.G.; Faymonville M.L.; Messmer B.J.; Buro- Rathsmann K.; Von Bernuth G.  
 CORPORATE SOURCE: Department of Pediatric Cardiology, RWTH Aachen, Pauwelsstrasse, 52057 Aachen, Germany  
 SOURCE: Journal of Thoracic and Cardiovascular Surgery, (1993) 106/6 (978-987).  
 ISSN: 0022-5223 CODEN: JTCSAQ

COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery  
018 Cardiovascular Diseases and Cardiovascular Surgery  
025 Hematology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Twenty-nine children 3 months to 17 years of age undergoing operations for congenital heart disease were included in this prospective study. Complement activation, activation of the plasma contact system, leukocytes, leukocyte elastase release, and C-reactive protein were studied during and after cardiopulmonary bypass for the first postoperative week and related to multiple system organ failure occurring in eight (27.5 %) of the 29 children. During cardiopulmonary bypass complement activation via the alternative pathway as indicated by significant conversion of C3 (expressed by C3d/C3) and abnormally high C5a values at the end of cardiopulmonary bypass without consumption of C4 was shown in all children. At the end of cardiopulmonary bypass, C3 conversion was significantly higher in the eight patients with multiple system organ failure than in the others ( $p < 0.05$ ), whereas no difference in C5a level was shown. All children had a significant increase in leukocyte count directly after protamine administration ( $p < 0.0001$ ) and elastase release during cardiopulmonary bypass that was significantly higher in patients with multiple system organ failure than in those without ( $p < 0.05$ ). Consumption of prekallikrein as an indicator of activation of the Hageman system was not **detectable** during **cardiopulmonary** bypass in any child. After cardiopulmonary bypass, in patients without multiple system organ failure, C3d/C3 decreased and reached preoperative values within the first postoperative week, whereas, in patients with multiple system organ failure, C3d/C3 increased further, reaching a maximal value on the third postoperative day. In comparison with patients without multiple system organ failure, patients with multiple system organ failure showed a severe decrease of C4 (with minimal values on the third postoperative day), suggesting consumption by activation of the classic pathway of the complement system or a hepatic synthesis deficiency. Prekallikrein values were also significantly lower in patients with multiple system organ failure than in the others, with a maximal difference on the third postoperative day ( $p < 0.005$ ). C-reactive protein was significantly lower in patients with multiple system organ failure than in the others for the first 2 postoperative days ( $p < 0.05$ ), probably because of severe hepatic failure in patients with multiple system organ failure. This study demonstrates that, in children, cardiopulmonary bypass induces complement activation principally via the alternative pathway. It suggests a relationship between complement activation and multiple system organ failure observed in the postoperative period. Furthermore, it points out the role of multiple system organ failure itself on the C3 conversion and on the synthesis of the markers of the inflammatory response in children after heart operations.

L35 ANSWER 61 OF 87 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1993:454851 BIOSIS

DOCUMENT NUMBER: PREV199396099751

TITLE: Supervised exercise training improves cardiopulmonary fitness in HIV-infected persons.

AUTHOR(S): MacArthur, Rodger D.; Levine, Sheldon D. (1); Birk, Thomas J.

CORPORATE SOURCE: (1) Total Rehabilitation Athletic Conditioning Cent., Novi, MI USA

SOURCE: Medicine and Science in Sports and Exercise, (1993) Vol.

25, No. 6, pp. 684-688.  
ISSN: 0195-9131.

DOCUMENT TYPE: Article  
LANGUAGE: English

AB We attempted to **measure cardiopulmonary** effects, CD4 counts, and perceived sense of well-being in 25 individuals moderately to severely immunocompromised from HIV infection (mean entry CD4 count = 144  $\pm$  11) before and after a 24-wk program of exercise training. Only six subjects completed the 24-wk program. All six showed evidence of a training effect. Statistically significant improvements were seen in maximal oxygen consumption ( $\dot{V}O_{2max}$ ), oxygen pulse, and minute ventilation. Submaximal exercise performance improved significantly by 12 wk in the 10 individuals available for testing: decreases were seen in heart rate, rate pressure product, and rate of perceived exertion. White blood cell counts and T-lymphocyte subsets were stable at 12 and 24 wk in the subjects available for testing. High depression/anxiety scores on a mental health inventory (General Health Questionnaire) correlated with low CD4 counts. Scores did not correlate with compliance with the exercise program. There was a trend ( $P < 0.10$ ) for scores to improve over time among those individuals who attended  $\geq 80\%$  of scheduled exercise sessions. We conclude that exercise training is feasible and beneficial for some HIV-infected individuals.

L35 ANSWER 62 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:496141 HCAPLUS

DOCUMENT NUMBER: 119:96141

TITLE: Cyclic disulfide analogs of the **complement** component **C3a**: synthesis and conformational investigations

AUTHOR(S): Pohl, Martina; Ambrosius, Dorothee; Groetzinger, Joachim; Kretzschmar, Titus; Saunders, Derek; Wollmer, Alex; Brandenburg, Dietrich; Bitter-Suermann, Dieter; Hoecker, Hartwig

CORPORATE SOURCE: Ger. Wool Res. Inst., Aachen, Germany

SOURCE: International Journal of Peptide & Protein Research (1993), 41(4), 362-75

CODEN: IJPPC3; ISSN: 0367-8377

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

R-Cys-X-X-Leu-Cys-Leu-Ala-Arg-OH I

AB Twenty-six cyclic disulfide bridge analogs of the anaphylatoxic peptide C3a were prep'd. to elucidate the receptor binding conformation of the C-terminal region, as well as to examine a synthetic approach to potential antagonists. Solid phase peptide synthesis was performed on different polymeric supports by individual peptide synthesis, with 9-fluorenylmethoxycarbonyl (Fmoc) strategy, and simultaneous multiple peptide synthesis, using tert-butoxycarbonyl (Boc) and Fmoc strategies. Both strategies gave open-chain peptides in comparable yields. Syntheses using the Boc strategy employed the HF-labile 4(methoxy)benzyl group (Mob) for  $\beta$ -thiol protection of cysteine; in contrast, the CF<sub>3</sub>CO<sub>2</sub>H-stable protecting groups, acetamidomethyl (Acm) and trityl (Trt), were chosen for

syntheses employing Fmoc strategy. Ring closure reactions by iodine oxidn. were carried out starting from protected (Acm/Acm, Trt/Acm) or unprotected dithiols. The resulting cyclic C3a analogs were characterized by HPLC, amino acid anal., and fast-atom-bombardment **mass spectrometry**. Conformational investigations using CD and theor. structural investigations by mol. dynamics calcns. revealed that slight variations in sequence result in pronounced conformational consequences. The potential of cyclic C3a analogs to activate or to desensitize guinea pig platelets, a std. test system for biol. activities of anaphylatoxic peptides like C3a, revealed relatively low activities for cyclic peptides (<0.1% C3a activity). N-terminal acylation with cationic, arginine-rich sequences like Tyr-Arg-Arg-Gly-Arg led to amplified biol. effects. Three peptides I [R = H, X = Ala; R = H-Tyr-Arg-Arg-Gly-Arg-NH(CH<sub>2</sub>)<sub>5</sub>CO, H-Tyr-Arg-Arg-Gly-Arg, X = Gly] point in the direction of C3a antagonists.

L35 ANSWER 63 OF 87 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
24

ACCESSION NUMBER: 1993:91417 BIOSIS

DOCUMENT NUMBER: PREV199395046613

TITLE: Effects of double-filtration plasmapheresis and a platelet-activating factor antagonist on the prolongation of xenograft survival.

AUTHOR(S): Taniguchi, Shigeki (1); Kitamura, Soichiro; Kawachi, Kanji; Fukutomi, Masaaki; Yoshida, Yoshitsugu; Kondo, Yoshiaki

CORPORATE SOURCE: (1) Dep. Surg. III, Nara Med. Coll., 840 Shijo-cho, Kashihara, Nara 634 Japan

SOURCE: Journal of Heart and Lung Transplantation, (1992) Vol. 11, No. 6, pp. 1200-1208.  
ISSN: 1053-2498.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Xenotransplantation may be considered a possible solution to the clinical donor-organ shortage. We studied the effects of the removal of preformed natural antibodies against donor tissue by double-filtration plasmapheresis (DFPP) and the administration of a platelet-activating factor antagonist on the prolongation of xenograft survival using the pig-to-dog model. The porcine hearts were perfused with the blood of mongrel dogs. Pairs of animals were divided into four groups: group I (n=3) was given no pretreatment before perfusion; group II (n=6) was pretreated by DFPP; group III (n=3) was given a platelet-activating factor antagonist intravenously at a dose of 0.1 mg/kg 5 minutes before and after perfusion; group IV (n=5) was pretreated by DFPP and then given a platelet-activating factor antagonist. The titer of natural antibodies was **measured** by lymphocytotoxicity and hemagglutination. **Heart** specimens were examined by immunohistochemical staining for deposits of dog antibodies. No immunosuppressive drugs were given in this study. The porcine hearts resumed beating immediately after perfusion in all groups. The mean duration of the graft beating was 17.0+-2.0 minutes for group I, 215.2+-22.6 minutes for group II (p lt 0.001 compared with group I), 18.3+-2.1 minutes for group III, and 317.0+-26.5 minutes for group IV (p lt 0.001 compared with group II). Immunoglobulin (Ig) M, IgG, complements (C3, C4), and fibrinogen were removed significantly from the perfusing blood, and natural antibody titer was scarcely **detectable** in groups II and IV after DFPP. According to histologic findings, deposition of dog IgM to the coronary artery wall of the porcine heart was more evident in groups I and III than in the other two groups. The suggestion was that the duration of survival of the porcine heart in this xenotransplantation model could be extended by the concomitant use of DFPP and a platelet-activating factor antagonist.

L35 ANSWER 64 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 25  
ACCESSION NUMBER: 1992:589843 HCAPLUS  
DOCUMENT NUMBER: 117:189843  
TITLE: Western blot analysis of human IgG reactive with the  
collagenous portion of Clq: evidence of distinct  
binding specificities  
AUTHOR(S): Maartensson, U.; Sjoeholm, Andres G.; Sturfelt, G.;  
Truedsson, L.; Laurell, A. B.  
CORPORATE SOURCE: Dep. Med. Microbiol., Lund Univ., Lund, Swed.  
SOURCE: Scandinavian Journal of Immunology (1992), 35(6),  
745-50  
CODEN: SJIMAX; ISSN: 0300-9475  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB An ELISA with purified collagenous complement Clq fragments in the solid  
phase was used for **detection** of Clq-specific Igs in the sera of  
patients with systemic lupus erythematosus (SLE) or the SLE-like disease  
hypocomplementemic urticarial vasculitis syndrome (HUVS). All patients  
demonstrated high concns. of Clq-specific IgG and markedly low concns. of  
circulating Clq. **Detection** of Clq-specific IgG in SLE sera was  
facilitated by employment of satg. concns. of collagenous Clq fragments in  
the solid-phase ELISA. When added to SLE serum, immune complex-fixed Clq  
inhibited binding of IgG to the Clq fragments, whereas addn. of Clq alone  
had limited inhibitory effects. No ELISA inhibition was obsd. after addn.  
of Clq or immune complex-fixed Clq to a HUVS serum. Thus, possible  
interactions between HUVS-IgG and native Clq are probably of low affinity.  
By Western blot anal., IgG reactive with the B and C chains of Clq was  
found in the 8 patients with evidence of HUVS, 5 of whom also showed IgG  
binding to C'-C' and A'-B' dimers of collagenous Clq fragments. Sera from  
SLE patients were neg. by Western blot anal. Apparently, Clq-specific IgG  
in SLE primarily recognizes assembled Clq mols. or collagenous Clq  
fragments expressing conformational epitopes of bound Clq. There was no  
correlation between findings of Clq-specific IgG and a variety of  
autoantibodies assocd. with SLE and SLE-like disease.

L35 ANSWER 65 OF 87 MEDLINE DUPLICATE 26  
ACCESSION NUMBER: 93001242 MEDLINE  
DOCUMENT NUMBER: 93001242 PubMed ID: 1389244  
TITLE: Biocompatibility of extracorporeal circulation with  
autooxygenation.  
AUTHOR: Bochenek A; Religa Z; Kokot F; Wnuk-Wojnar A M; Wojnar J;  
Wnuk R; Gallert G; Skiba J  
CORPORATE SOURCE: 1st Clinic of Cardiac Surgery, Silesian Medical Academy,  
Silesian Heart Center, Katowice, Poland.  
SOURCE: EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY, (1992) 6 (8)  
397-402.  
Journal code: 8804069. ISSN: 1010-7940.  
PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199211  
ENTRY DATE: Entered STN: 19930122  
Last Updated on STN: 19980206  
Entered Medline: 19921112  
AB Platelet damage, complement activation and neutropenia during  
cardiopulmonary bypass are the result of blood contact with artificial  
surfaces, mainly in the oxygenator. To evaluate biocompatibility of this



kind of bypass we compared two techniques of extracorporeal circulation in 40 patients undergoing elective coronary bypass operations. In 20, a standard technique with a bubble oxygenator was used (group 1), and in the remaining 20 patients with autooxygenation, the patients' own lungs were included in the perfusion circuit (group 2). Several blood samples were taken before, during and after perfusion to estimate the corrected platelet numbers and pulmonary leucocyte sequestration in all patients, and additionally in 6 patients from each group, **complement C3a** and **C5a** anaphylatoxins were **measured** (radioimmunoassay). At the end of **cardiopulmonary** bypass, the decline of platelet number corrected to haematocrit platelet number in group 1 was significantly higher than in group 2 (P less than 0.01). There was a significant increase in circulating white blood cells when compared to pre-bypass time in both groups (P less than 0.05). However, comparison of differences between leucocyte counts in the blood of the patients' right and left atria showed enhanced leucocyte sequestration in group 1,  $1.46 \pm 0.5 \times 10^3/\text{mm}^3$  vs only  $0.34 \pm 0.2 \times 10^3/\text{mm}^3$  in group 2. The **C3a** rose progressively during extracorporeal circulation: in group 1 from  $268 \pm 46 \text{ ng/l}$  to  $521 \pm 65 \text{ ng/l}$ , and in group 2 from  $244 \pm 46 \text{ ng/l}$  to  $418 \pm 34 \text{ ng/l}$  (P less than 0.05). No characteristic changes in **C5a** activation were observed in either group. (ABSTRACT TRUNCATED AT 250 WORDS)

L35 ANSWER 66 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 93164033 EMBASE  
 DOCUMENT NUMBER: 1993164033  
 TITLE: The assessment of protamine and perfusion related immunologic effects with complement, thromboxane and leucocyte parameters.  
 AUTHOR: Durak P.; Ozgok A.; Erdemli O.; Ebil S.  
 CORPORATE SOURCE: Anesteziyol. ve Reanimasyon Klinigi, Turkiye Yuksek Ihtisas Hastanesi, Ankara, Turkey  
 SOURCE: Turk Anesteziyoloji ve Reanimasyon, (1992) 20/6 (392-397). ISSN: 1016-5150 CODEN: TANREP  
 COUNTRY: Turkey  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 024 Anesthesiology  
 026 Immunology, Serology and Transplantation  
 030 Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: Turkish  
 SUMMARY LANGUAGE: English; Turkish  
 AB This study was planned in order to find out the probable immunologic reactions due to perfusion and protamine infusion and to follow up these reaction periods with specific parameters like **complement** (**C3**), (**C4**), (**C5**), thromboxane B2 (Trx B2) and leucocyte counts. Total intravenous anaesthesia was used in these 20 patients who had been scheduled for this study. Patients were premedicated with morphine 10 mg. IM and diazepam 10 mg. PO. Fentanyl+diazepam+pancuronium was used for induction. Fentanyl+pancuronium were the agents of maintenance and 4 mg/kg heparin was used and the patients were neutralized with same amount of protamine through the central venous catheter in 10 minutes time. Blood samples were taken for Trx B2, (**C3**), (**C4**), (**C5**), arterial blood gases and complete blood count. The samples were taken and **cardiac** output was **measured** just after the induction, before and 10 minutes after the protamine infusion. For the leucocyte count, blood samples were taken both from arterial and venous catheters. It was seen that venous leucocyte count was considerably high after protamine infusion ( $p < 0.01$ ). This was positively correlated with Trx B2 values ( $p < 0.05$ ). The number of platelets were also decreased after protamine infusion ( $p < 0.05$ ). The

increases in complements (C3), (C4), (C5) were statistically significant during by-pass. It is concluded that (C3), (C4), (C5) values are to be followed specially during bypass. As for protamine, following up the arterial-venous leucocyte counts with Trx can be a kind of immunologic reaction follow up during and after protamine infusion.

L35 ANSWER 67 OF 87 MEDLINE DUPLICATE 27  
 ACCESSION NUMBER: 92250320 MEDLINE  
 DOCUMENT NUMBER: 92250320 PubMed ID: 1577619  
 TITLE: Immunofluorescent localization of pig complement component 3, regardless of the presence or absence of **detectable** immunoglobulins, in hyperacutely rejected **heart** xenografts.  
 AUTHOR: Wang M W; Johnston P S; Wright L J; Lim S M; White D J  
 CORPORATE SOURCE: Department of Surgery, University of Cambridge Clinical School, Addenbrooke's Hospital, UK.  
 SOURCE: HISTOCHEMICAL JOURNAL, (1992 Feb) 24 (2) 102-9.  
 Journal code: 0163161. ISSN: 0018-2214.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199206  
 ENTRY DATE: Entered STN: 19920619  
 Last Updated on STN: 19980206  
 Entered Medline: 19920610

AB Rabbit heart xenografts transplanted into the neck of newborn pigs were all hyperacutely rejected within two hours regardless of the presence or absence of **detectable** endogenous immunoglobulins (Ig). Cryostat tissue sections were prepared from the rejected rabbit hearts and incubated with sheep polyclonal antibodies against pig **complement** component 3 (C3), pig IgG and pig IgM. Specific immunoreaction was visualized by fluorescein-conjugated antibodies to sheep IgG. C3 was localized mainly on the surfaces of vascular endothelial as well as myocardial cells, and the localization was not dependent upon the presence of pig immunoglobulins within the same tissue. Both pig IgG and IgM were **detected** only in the **heart** xenografts transplanted into suckled pigs, whereas no trace of immunoglobulin was found in those transplanted into circulating antibody-free presuckled pigs. Treatment with cobra venom factor (which inhibits complement activity) prior to transplantation prolonged xenograft survival and completely abolished C3 immunostaining. The results provide new evidence at the histochemical level that the alternative pathway of complement is involved in hyperacute xenograft rejection of the species combination (rabbit to pig) used in this study.

L35 ANSWER 68 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 92145280 EMBASE  
 DOCUMENT NUMBER: 1992145280  
 TITLE: Transient endotoxaemia during cardiac surgery.  
 AUTHOR: Andersen L.W.; Baek L.  
 CORPORATE SOURCE: Department of Anaesthesia, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark  
 SOURCE: Perfusion, (1992) 7/1 (53-58).  
 ISSN: 0267-6591 CODEN: PERFER  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 004 Microbiology  
 005 General Pathology and Pathological Anatomy

018 Cardiovascular Diseases and Cardiovascular Surgery  
 037 Drug Literature Index  
 052 Toxicology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Within the past few years, several studies have demonstrated the presence of circulating endotoxin during open-heart surgery. Methods for the **detection** of endotoxin have become more specific and more sensitive. Endotoxins are responsible for activation of numerous harmful biological mediators that result in a systemic inflammatory response that is accompanied by direct cellular injury in different organ systems. We and others have proposed that endotoxin partially accounts for this CPB-induced systemic inflammatory response. The clinical significance of transient endotoxaemia associated with cardiac surgery procedures remains to be determined

L35 ANSWER 69 OF 87 MEDLINE DUPLICATE 28  
 ACCESSION NUMBER: 91275543 MEDLINE  
 DOCUMENT NUMBER: 91275543 PubMed ID: 2055075  
 TITLE: Immune dysfunction in children after corrective surgery for congenital heart disease.  
 COMMENT: Comment in: Crit Care Med. 1992 Apr;20(4):554-5  
 AUTHOR: Hauser G J; Chan M M; Casey W F; Midgley F M; Holbrook P R  
 CORPORATE SOURCE: Department of Critical Care Medicine, Georgetown University Children's Medical Center, Washington, DC 20007.  
 SOURCE: CRITICAL CARE MEDICINE, (1991 Jul) 19 (7) 874-81.  
 Journal code: 0355501. ISSN: 0090-3493.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 ENTRY MONTH: 199108  
 ENTRY DATE: Entered STN: 19910818  
 Last Updated on STN: 19980206  
 Entered Medline: 19910801

AB OBJECTIVE: To study the effect of open- and closed-heart surgery on the immune status of infants and children. DESIGN: Prospective study. Data collected before anesthesia and surgery and 2 and 24 hrs after surgery. SETTING: Operating room and pediatric ICU in a children's hospital. PATIENTS: Children undergoing surgery for correction of congenital heart disease (age 3 months to 12 yrs). A total of 31 patients were studied (open-heart surgery, n = 25; closed-heart surgery, n = 6). **MEASUREMENTS AND MAIN RESULTS:** Increased neutrophil counts and lymphopenia were observed after both open- and closed-heart surgery. Serum levels of the **complement** components C3 and C4 were depressed after open-heart surgery, but not after closed procedures. The percentage of T3+ and T4+ lymphocytes, proliferative responses of the lymphocytes and serum immunoglobulin (Ig)G and IgM were decreased from preoperative levels after open-heart surgery. The percentage of T8+ lymphocytes and serum IgA levels did not change. Intraoperative variables and postoperative severity of illness (Pediatric Risk of Mortality score) did not correlate with immune suppression. **CONCLUSIONS:** The immune system is affected after pediatric cardiac surgery, particularly after open-heart surgery.

L35 ANSWER 70 OF 87 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 1992:56803 HCAPLUS  
 DOCUMENT NUMBER: 116:56803  
 TITLE: Molecular epitope identification of the anaphylatoxin

**C3a complement by mass spectrometric** peptide mapping using an immobilized antigen-antibody complex

AUTHOR(S): Suckau, D.; Koehl, J.; Karwath, G.; Schneider, K.; Bitter-Suermann, D.; Przybylski, M.

CORPORATE SOURCE: Fac. Chem., Univ. Konstanz, Konstanz, D-7750, Germany

SOURCE: Pept. 1990, Proc. Eur. Pept. Symp., 21st (1991), Meeting Date 1990, 356-8. Editor(s): Giralt, Ernest; Andreu, David. ESCOM Sci. Publ.: Leiden, Neth. CODEN: 57HNAI

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Results are presented of epitope extn. and 252Cf-plasma desorption **mass spectrometry** (PDMS) anal. using mixts. of several model peptides, which confirm and exactly define the C-terminal epitope sequences of **complement C3a**.

L35 ANSWER 71 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1991:60111 HCAPLUS

DOCUMENT NUMBER: 114:60111

TITLE: Molecular epitope identification by limited proteolysis of an immobilized antigen-antibody complex and **mass spectrometric** peptide mapping

AUTHOR(S): Suckau, Detlev; Koehl, Joerg; Karwath, Gabriele; Schneider, Klaus; Casaretto, Monika; Bitter-Suermann, Dieter; Przybylski, Michael

CORPORATE SOURCE: Fak. Chem., Univ. Konstanz, Konstanz, D-7750, Germany

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1990), 87(24), 9848-52 CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Sequences of antigenic determinants were identified by limited proteolysis of peptide antigens bound to an immobilized monoclonal antibody and direct mol. wt. detn. of the monoclonal antibody-bound peptide fragments by 252Cf plasma desorption **mass spectrometry**. The epitope peptides to the monoclonal antibody h453 [Burger, R., et al, 1988] were isolated from immobilized antigen-antibody complexes by partial trypsin digestion. A synthetic eicosapeptide comprised of the C-terminal sequence of the human complement component polypeptide des-Arg77-C3a as well as guinea pig des-Arg78-C3a was used as an antigen. Conditions were developed under which trypsin specifically degraded the antigens without inactivation of the immobilized antibody. After proteolysis, epitope peptides were dissocd. from the antibody with 4 M MgCl2. The antigenic peptides were purified by HPLC and identified by 252Cf plasma desorption **mass spectrometry**. The epitope recognized by h453 resides on the C-terminal tryptic peptides of human (residues 70-76) and guinea pig (residues 70-77) C3a. As an estn. of accuracy this method is able to provide, trypsin digestion of immune complexes caused cleavage of the antigen within a distance of 2 amino acid residues upstream from the epitope.

L35 ANSWER 72 OF 87 MEDLINE

ACCESSION NUMBER: 90297969 MEDLINE

DOCUMENT NUMBER: 90297969 PubMed ID: 2361017

TITLE: Complement activation before, during and after cardiopulmonary bypass.

AUTHOR: Bonser R S; Dave J R; John L; Gademsetty M K; Carter P G;

CORPORATE SOURCE: Davies E; Taylor P; Gaya H; Lennox S C; Vergani D  
 SOURCE: Department of Surgery, Brompton Hospital, London, UK.  
 EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY, (1990) 4 (6)  
 291-6.  
 Journal code: 8804069. ISSN: 1010-7940.  
 PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199008  
 ENTRY DATE: Entered STN: 19900907  
 Last Updated on STN: 19990129  
 Entered Medline: 19900806

AB Plasma levels of the **complement** parent molecules C3, C4, and factor B and their split products, C3d, C4d, and Ba were **measured** in 12 patients undergoing **cardiopulmonary** bypass for coronary artery surgery. Alternative and common complement pathway activation, demonstrated by statistically significant rising levels of Ba (P less than 0.05), and C3d (P less than 0.05) and by elevated Ba:B (P less than 0.05) and C3d:C3 (P less than 0.05) ratios were found before the institution of cardiopulmonary bypass but following heparin administration suggesting that heparin may itself initiate alternative pathway activation. In addition, significant depletion of parent complement components and elevation of split product concentrations was seen during bypass suggesting classical and alternate pathway activation (P less than 0.01). This study clarifies the pathways of complement activation during bypass and presents evidence that heparin administration may initially activate the complement cascade.

L35 ANSWER 73 OF 87 MEDLINE DUPLICATE 29  
 ACCESSION NUMBER: 90237315 MEDLINE  
 DOCUMENT NUMBER: 90237315 PubMed ID: 2332539  
 TITLE: Value of C-reactive protein in reflecting the magnitude of complement activation in children undergoing open heart surgery.  
 AUTHOR: Aronen M; Leijala M; Meri S  
 CORPORATE SOURCE: Children's Hospital, Finland.  
 SOURCE: INTENSIVE CARE MEDICINE, (1990) 16 (2) 128-32.  
 Journal code: 7704851. ISSN: 0342-4642.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199006  
 ENTRY DATE: Entered STN: 19900706  
 Last Updated on STN: 19980206  
 Entered Medline: 19900607

AB The kinetics of C-reactive protein (CRP) were studied prospectively in 30 children (aged 21 days - 16 years) undergoing open heart surgery. CRP was related to the kinetics of total haemolytic **complement**, **complement C3a** and postoperative complications. Two (7%) patients died and ten (33%) had postoperative complications. The patients with complications were younger (p less than 0.035), underwent longer perfusions (p less than 0.001) and had longer aortic cross-clamping times (p less than 0.003). The mean peak CRP level after surgery (108 mg/l) was reached, on the average, in 43 h. No statistical difference in CRP concentrations was found between the complication and non-complication groups. Extensive complement activation was seen in every patient. CRP did not reflect the magnitude of complement activation induced by

cardiopulmonary bypass. The patient sample was too small to draw reliable conclusions about the value of CRP in **detecting** postoperative complications after open **heart** surgery in children.

L35 ANSWER 74 OF 87 MEDLINE DUPLICATE 30  
 ACCESSION NUMBER: 89363521 MEDLINE  
 DOCUMENT NUMBER: 89363521 PubMed ID: 2770325  
 TITLE: The role of neural and vasoactive mediators in the regulation of the pulmonary circulation during cardiopulmonary preservation.  
 AUTHOR: Mashburn J P; Kontos G J Jr; Hashimoto K; Wilson D M; Schaff H V  
 CORPORATE SOURCE: Mayo Clinic, Rochester, MN 55905.  
 SOURCE: JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY, (1989 Sep) 98 (3) 434-42; discussion 442-3.  
 Journal code: 0376343. ISSN: 0022-5223.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 ENTRY MONTH: 198909  
 ENTRY DATE: Entered STN: 19900309  
 Last Updated on STN: 19900309  
 Entered Medline: 19890925

AB The autoperfused working heart-lung preparation has been used for extended cardiopulmonary preservation for transplantation. However, acute lung injury and failure of the preparation can result from pulmonary hypertension, which previous investigators have linked to denervation. We studied the neural and vasoactive mediators of pulmonary vasoconstriction during normothermic autoperfusion of the heart and lungs from 13 calves. Pulmonary vascular resistance was quantitated by multipoint pulmonary artery pressure/flow plots generated by incremental reduction in venous return at three times: A, after sternotomy but before autoperfusion (control); B, during in situ autoperfusion (innervated heart-lung preparation); and C, after explanation (denervated **heart-lung** preparation). During hemodynamic **measurements**, left atrial blood samples were obtained for **measurement** of thromboxane B2, 6-keto-prostaglandin-F1 alpha, and **complement** activation products **C3a** and C5a. Results show that pulmonary hypertension in the autoperfused working heart-lung preparation begins during autoperfusion before denervation and may be related to complement activation and to increased levels of circulating thromboxane B2 and 6-keto-prostaglandin F1 alpha (both the absolute levels and the ratio of thromboxane B2 to 6-keto-prostaglandin F1 alpha). After denervation, both prostaglandin intermediates were markedly increased, but their ratio was not significantly affected. These data suggest that there is an initial stage of pulmonary vasoconstriction at the onset of autoperfusion that is accompanied by increased circulating levels of vasoactive mediators and that denervation further contributes to this response.

L35 ANSWER 75 OF 87 MEDLINE DUPLICATE 31  
 ACCESSION NUMBER: 89176912 MEDLINE  
 DOCUMENT NUMBER: 89176912 PubMed ID: 2466945  
 TITLE: **Diagnostic** validity of multivariate combinations of biochemical analytes as markers for rejection and infection in the follow-up of patients with heart transplants.  
 AUTHOR: Holzel W G; Havel M; Laczkovics A; Muller M M  
 CORPORATE SOURCE: Institut fur Pathologische und Klinische Biochemie,

SOURCE: Humboldt-Universitat Berlin, Charite, GDR.  
JOURNAL OF CLINICAL CHEMISTRY AND CLINICAL BIOCHEMISTRY,  
(1988 Nov) 26 (11) 667-71.  
Journal code: 7701860. ISSN: 0340-076X.  
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198905  
ENTRY DATE: Entered STN: 19900306  
Last Updated on STN: 19980206  
Entered Medline: 19890511

AB The **diagnostic** validity of multivariate combinations of alpha 1-antitrypsin, alpha 2-macroglobulin, C-reactive protein, **complement C3**, **complement C4**, neopterin in serum, and neopterin in urine as markers for acute **cardiac** allograft rejection and for differential **diagnosis** of rejection and infections was investigated in the follow-up of 37 patients with **heart** transplants. Rejection was **diagnosed** by endomyocardial biopsy. Infections were classified as 'no infection', 'viral infection', and 'bacterial, fungal or mixed infections'. Although there are significant differences between the mean levels of analytes, multivariate discriminant analysis does not provide an adequate discrimination of rejection and infection states. In separate rejection **diagnosis**, multivariate combinations of analytes cannot replace endomyocardial biopsy. However, a multivariate combination of alpha 1-antitrypsin, alpha 2-macroglobulin, C-reactive protein, C3, C4 in serum, and neopterin in urine can be used as a screening procedure to reduce the number of endomyocardial biopsies.

L35 ANSWER 76 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1989:528692 HCAPLUS  
DOCUMENT NUMBER: 111:128692  
TITLE: Carcinogen attachment to serum proteins  
AUTHOR(S): Orley, C.; Tapon, J.  
CORPORATE SOURCE: Cent. Tech. Soutien Rech., Villejuif, 94801, Fr.  
SOURCE: Optica Pura y Aplicada (1988), 21(2), 101-5  
CODEN: OPAPAY; ISSN: 0030-3917  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Electron microscopy and **mass spectrometry** were used for identifying the chem. bonds of methyl-naphthobenzacridine (MNBA)-labeled .alpha.2-macroglobulin, complement factors, and Igs. Electron microscopy revealed that .alpha.2-macroglobulin exists in an open and closed form, corresponding to the native and enzyme-bound protein. With **mass spectrometry**, it was demonstrated that a thiol ester formed from glutamic acid and cysteine is covalently bound to the NH2 of the MNBA. .alpha.2-Macroglobulin and **complement C3** and C5 of blood have a common precursor contg. a thiol ester that can bind with the proteases and the carcinogens. In IgG and IgM, distinct peaks indicate noncovalent binding of tryptophan and tyrosine. A possible explanation for the observations is presented.

L35 ANSWER 77 OF 87

MEDLINE

DUPLICATE 32

ACCESSION NUMBER: 85137523 MEDLINE  
DOCUMENT NUMBER: 85137523 PubMed ID: 3844601  
TITLE: Carbohydrate composition of the second, third and fifth components and factors B and D of human complement.  
AUTHOR: Tomana M; Niemann M; Garner C; Volanakis J E

CONTRACT NUMBER: AI-15607 (NIAID)  
AI-21067 (NIAID)  
AM-03555 (NIADDK)

+

SOURCE: MOLECULAR IMMUNOLOGY, (1985 Feb) 22 (2) 107-11.  
Journal code: 7905289. ISSN: 0161-5890.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198504  
ENTRY DATE: Entered STN: 19900320  
Last Updated on STN: 19990129  
Entered Medline: 19850419

AB The carbohydrate composition of the second, third and fifth components of human **complement** (C2, C3 and C5) and of factors B and D was determined employing gas-chromatographic and **mass-spectrometric** methods. C2 was found to contain 15.9% carbohydrate composed of fucose, galactose, mannose, N-acetylglucosamine and N-acetylneuraminate (approximate molar ratio 1:4:9:9:4). N-acetylglucosamine and mannose (approximate molar ratio 1:4), amounting to 1.7% of the mass of the molecule, were the only monosaccharides **detected** in C3. C5 contained 3.8% carbohydrate composed of galactose, mannose, N-acetylglucosamine and N-acetylneuraminate (approximate molar ratio 2:4:4-5:2). The carbohydrate moiety of B consisted of fucose, galactose, mannose, N-acetylglucosamine and N-acetylneuraminate (molar ratio 1:2:3:4:2). The total carbohydrate content of B was estimated at 8.6%. In addition to these monosaccharides, glucose (0.4-0.9%) was also **detected** in all preparations analysed. Glucose was the only sugar **detected** in D.

L35 ANSWER 78 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 84098419 EMBASE  
DOCUMENT NUMBER: 1984098419  
TITLE: Evidence for the involvement of coupling factor B in the H<sup>+</sup> channel of the mitochondrial H<sup>+</sup>-ATPase.  
AUTHOR: Rao Sanadi D.; Pringle M.; Kantham L.; et al.  
CORPORATE SOURCE: Department of Cell Physiology, Boston Biomedical Research Institute, Boston, MA 02114, United States  
SOURCE: ISOTOPENPRAXIS, (1984) 20/1 (371-1374).  
CODEN: IPRXA  
COUNTRY: Germany  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 029 Clinical Biochemistry  
LANGUAGE: English

AB Membrane energization by ATP has been **measured** in vesicles containing purified bovine **heart** mitochondrial H<sup>+</sup>-ATPase (ATP synthase) with the voltage-sensitive dye oxonol VI. The dithiol chelator, Cd<sup>2+</sup>, and the thiol oxidant, copper o-phenanthroline, produced discharge of the membrane potential when added at the steady state and inhibited its establishment when added prior to energization by ATP. These effects, which were reversed by dithiothreitol, were not accompanied by an increase in the nonspecific H<sup>+</sup> permeability of the membrane. Passive H<sup>+</sup> conduction in proteoliposomes containing F<sub>0</sub> (hydrophobic segment of ATP synthase) was **assayed** by the quenching of 9-aminoacridine fluorescence after establishing a K<sup>+</sup> diffusion potential. This conductance was blocked by Cd<sup>2+</sup>, an inhibitor of coupling factor B(F<sub>B</sub>). Labeling of F<sub>0</sub> with <sup>115</sup>Cd<sup>2+</sup> at the concentrations that inhibited the F<sub>0</sub> conductance followed by gel electrophoresis yielded a single radioactive band with a molecular weight



corresponding to F(B), the presence of which in the F0 preparation was confirmed by immunoblot staining. The data offer strong evidence that F(B) is an essential component of the H<sup>+</sup> channel of F0, because H<sup>+</sup> conduction through the channel is inhibited by chemical modification of F(B).

L35 ANSWER 79 OF 87 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1984:283095 BIOSIS

DOCUMENT NUMBER: BA78:19575

TITLE: SEROLOGY AND TISSUE LESIONS IN RABBITS IMMUNIZED WITH STREPTOCOCCUS-MUTANS.

AUTHOR(S): STINSON M W; NISENGARD R J; NEIDERS M E; ALBINI B

CORPORATE SOURCE: DEP. MICROBIOLOGY, SCH. MED., STATE UNIV. N.Y., BUFFALO, NY 14214.

SOURCE: J IMMUNOL, (1983) 131 (6), 3021-3028.

CODEN: JOIMA3. ISSN: 0022-1767.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Rabbits were immunized i.v. or i.d. [intradermally] with sterile suspensions of disrupted *S. mutans* strain MT703 or K1R. Indirect immunofluorescence **assays** indicated that sera from 4 of 10 rabbits immunized i.d. contained antibodies reactive with monkey and human heart and kidney components; 19 of 24 rabbits immunized i.v. had antibodies reactive with these tissues. **Heart-reactive** antibodies were also **detected** by immunoelectrophoresis and indirect radioimmunoassay. These antibodies were absorbed well by cytoplasmic membranes, a whole cell extract and an alkali extract of *S. mutans* but only weakly by intact bacteria. Between 6-8 wk after the 1st i.v. administration of *S. mutans* vaccines, rabbits developed proteinuria and hematuria with subsequent weight loss and lethargy; .apprx. 25% of the animals died from illness between the 5th-6th mo. of immunization. In 13 of 15 rabbits, immune deposits of [complement] C3 and IgG, IgM or IgA and fibrinogen were seen in kidneys within the glomeruli, basement membranes of the peritubular capillaries and in the interstitium. In the heart, deposits were seen along the capillaries of the myocardium. In 8 of 14 rabbits, focal deposits of *S. mutans* antigen were **detected** in glomeruli and in the kidney interstitium. The kidneys showed gross pathologic and histopathologic changes. Most kidneys were pale and enlarged. Microscopic examinations revealed hypercellularity of the glomeruli, presence of neutrophils, thickening of glomerular and tubular basement membranes, tubular atrophy, edema and fibrosis of the interstitium. The kidney disease presented features of poststreptococcal glomerulonephritis. Microscopic examination of heart sections revealed mild perivascular infiltration by polymorphonuclear leukocytes and plasma cells in some of the rabbits.

L35 ANSWER 80 OF 87 MEDLINE DUPLICATE 33

ACCESSION NUMBER: 83237511 MEDLINE

DOCUMENT NUMBER: 83237511 PubMed ID: 6345466

TITLE: Rheumatic-like carditis induced in rabbits by cross-reacting antigens: Streptococcus A polysaccharide and rabbit aortic glycoproteins.

AUTHOR: Goldstein I; Scebat L; Renais J; Hadjinsky P; Dutartre J

SOURCE: ISRAEL JOURNAL OF MEDICAL SCIENCES, (1983 Jun) 19 (6) 483-90.

Journal code: 0013105. ISSN: 0021-2180.

PUB. COUNTRY: Israel

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198308  
 ENTRY DATE: Entered STN: 19900319  
 Last Updated on STN: 19900319  
 Entered Medline: 19830817

AB A rheumatic-like carditis was induced in rabbits by 8 mo of immunization with small doses of Streptococcus A polysaccharides or peptoglycane and rabbit aortic glycoprotein. **Cardiac** lesions were **detected** 5 to 6 mo after the beginning of immunization and were preceded by the appearance of circulating antibodies. The immunopathological study with peroxidase-labeled antibodies indicated the binding of IgG and **C3 complement** to the damaged cardiac areas. Enzyme-labeled antibodies to streptococcal polysaccharides were bound to the connective tissue of the cardiac valves and the coronary vessels. An immunological cross-reactivity was **detected** between Streptococcus A polysaccharide and aortic glycoprotein; this suggests that the immunopathological process initiated by the streptococcal infection may subsequently involve the cardiac tissue itself.

L35 ANSWER 81 OF 87 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1983:315315 BIOSIS  
 DOCUMENT NUMBER: BA76:72807  
 TITLE: IMMUNO PATHOLOGICAL STUDIES OF RATS INFECTED WITH ANGIOSTRONGYLUS-CANTONENSIS 1. CIRCULATING IMMUNE COMPLEXES AND DEPOSITION OF THE IMMUNE COMPLEXES ON THE TISSUES.  
 AUTHOR(S): TAKAI A  
 CORPORATE SOURCE: DEP. PARASITOL., SCH. MED., UNIV. RYUKYUS, NAHA, OKINAWA, 902 JPN.  
 SOURCE: ACTA MED BIOL, (1983) 30 (3-4), 105-124.  
 CODEN: AMBNAS. ISSN: 0567-7734.  
 FILE SEGMENT: BA; OLD  
 LANGUAGE: English

AB Circulating immune complexes (CIC) in the sera of rats infected with A. cantonensis were estimated by the precipitation method with 6% polyethylene glycol. The precipitates (PEG-ppt) increased remarkably after infection and in these PEG-ppt the antigen of A. cantonensis was frequently **detected** throughout the experiment. In the examinations of gel filtration on Sephadex G-200, PEG-ppt were **detected** in both the 1st and 2nd peaks, but the antigen was demonstrated only in the 2nd peak suggesting that the immune complexes were relatively low in MW. Total hemolytic **complement** and **C3** levels were found to fall as PEG-ppt increased during infection. Deposition of CIC in various tissues and histopathological changes in these areas were well observed in the infected rats. In the brains, the deposits of CIC were observed around the larvae in subarachnoid space and on the arterial walls. In such regions vasculitis with cellular infiltration was seen. Cardiac hypertrophy was found in rats later than 30 days after infection, and CIC were **detected** among **cardiac** muscles accompanying slight cellular infiltration. In the lungs, the findings of interstitial pneumonitis, severe vasculitis with retiform deposits of CIC were noted. Local depositions were also observed in pulmonary egg granulomas. Expansion of glomerular mesangial matrix was observed during 30 to 40 days after infection and CIC were positive in these glomeruli. The CIC may be formed between specific antibodies and antigens released from the worms and these CIC probably play a pathogenic role in various organs.

L35 ANSWER 82 OF 87 MEDLINE DUPLICATE 34  
 ACCESSION NUMBER: 83022805 MEDLINE  
 DOCUMENT NUMBER: 83022805 PubMed ID: 6982053

TITLE: Perioperative changes in complement associated with cardiopulmonary bypass.  
 AUTHOR: Boralessa H; Shifferli J A; Zaimi F; Watts E; Whitwam J G; Rees A J  
 SOURCE: BRITISH JOURNAL OF ANAESTHESIA, (1982 Oct) 54 (10) 1047-52. Journal code: 0372541. ISSN: 0007-0912.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 198212  
 ENTRY DATE: Entered STN: 19900317  
 Last Updated on STN: 19900317  
 Entered Medline: 19821216

AB The total haemolytic complement (CH50), the **complement** components **C3** and **C4**, the **complement** breakdown product **C3d**, alternative pathway activation and transferrin, were **measured** before, during and after **cardiopulmonary** bypass. As expected, CH50 decreased after heparinization, remained low during bypass and decreased further up to 8 h after bypass. **C3** and **C4** decreased significantly during bypass, continued to decrease for a further 8 h after bypass (by 35% and 40% respectively) and thereafter increased gradually up to 48 h. Although the depletions observed were suggestive of complement activation, there were no demonstrable increases in **C3d**, and in all patients the concentration of **C3d** remained within the normal range. Hence it was concluded that complement depletions of this magnitude were unlikely to result from complement activation. Non-specific changes in protein concentrations during bypass, as a result of dilution, redistribution or other unidentified factors, are more probable causes of the observed reductions. The acute phase response to surgery may be a factor in the subsequent increase in **C3** and **C4** which is seen 24 h after bypass. As transferrin concentrations in the plasma are known to decrease during this response the observed decrease in transferrin concentration would support this view.

L35 ANSWER 83 OF 87 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1980:530363 HCAPLUS  
 DOCUMENT NUMBER: 93:130363  
 TITLE: Methylamine reaction and denaturation-dependent fragmentation of complement component 3. Comparison with .alpha.2-macroglobulin  
 AUTHOR(S): Howard, James Bryant  
 CORPORATE SOURCE: Dep. Biochem., Univ. Minnesota, Minneapolis, MN, 55455, USA  
 SOURCE: Journal of Biological Chemistry (1980), 255(15), 7082-4  
 CODEN: JBCHA3; ISSN: 0021-9258  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB **Complement** protein **C3** can covalently incorporate [<sup>14</sup>C]methylamine with a stoichiometry of 0.85 mol/mol of protein. The reactive site is located in the larger, mol. wt. 135,000, peptide subunit of **C3**. The methylamine is incorporated as a deriv. of glutamic acid (.gamma.-glutamylmethylamide) which was identified by high-performance liq. chromatog. and low resolu. **mass spectroscopy**. **C3** went under a specific, denaturation-dependent protein fragmentation in SDS at 90.degree.. The cleavage results in the partial conversion of the mol. wt. 135,000 subunit to fragments of mol. wt. 84,000 and 53,000. The cleavage is completely prevented by reaction of **C3** with methylamine prior

to the 90.degree. incubation. The site of methylamine incorporation (the glutamyl residue) and the peptide fragmentation reaction have been reported for .alpha.2-macroglobulin (Howard, J. B., et al, 1980). A comparison of the results for the 2 proteins suggests that they have a common methylamine-reactive site.

L35 ANSWER 84 OF 87 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 35  
 ACCESSION NUMBER: 1979:572420 HCAPLUS  
 DOCUMENT NUMBER: 91:172420  
 TITLE: Physical stress and training in the elderly  
 AUTHOR(S): Liesen, H.; Dufaux, B.; Heck, H.; Mader, A.; Rost, R.;  
 Loetzerich, S.; Hollmann, W.  
 CORPORATE SOURCE: Inst. Kreislaufforsch. Sportmed., Cologne, Fed. Rep.  
 Ger.  
 SOURCE: Deutsche Zeitschrift fuer Sportmedizin (1979), 30(7),  
 218-20, 222, 224, 226  
 CODEN: DZSPD8; ISSN: 0344-5925  
 DOCUMENT TYPE: Journal  
 LANGUAGE: German

AB A discussion is given of the possibilities for improving phys. capacity in the elderly by phys. training, as seen from **measurements** of lactate, O uptake, **heart** frequency, and several indexes of energy metab. The ideal intensity of training for women >35 yr old apparently involves a level of stress which produces lactate levels in the blood of 3.5 mmol/L. An improved phys. performance can be achieved in endurance exercises 3 times per wk with uninterrupted exertion for 10-15 min at each session. However, more frequent (4 times per wk) and prolonged (30-40 min) exercise is needed for improvement in resistance to atherosclerosis and physiol. stress. O uptake capacity decreases with age in men, but trained subjects have significantly higher capacity than untrained subjects at all ages. In addn., muscle creatine kinase, phosphokexose isomerase, pyruvate kinase, and succinate and isocitrate dehydrogenases are all increased in by training in men 55-70 yr old. Ten wk of endurance training also eliminated the increase in serum levels of C3, C4, and C1 inhibitor occurring after exercise.

L35 ANSWER 85 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
 ACCESSION NUMBER: 79082795 EMBASE  
 DOCUMENT NUMBER: 1979082795  
 TITLE: [Changes in immune defenses after cardiac surgery under  
 extracorporeal circulation].  
 MODIFICATIONS DES DEFENSES IMMUNITAIRES APRES CHIRURGIE  
 CARDIAQUE FAITE SOUS CIRCULATION EXTRACORPORELLE.  
 AUTHOR: Gougerot-Pocidallo M.A.; Hakim J.; Lecompte Y.; Troube H.  
 CORPORATE SOURCE: Lab. Cent. Immunol. Hematol., Hop. Bichat, 75877 Paris 18,  
 France  
 SOURCE: Clinical Respiratory Physiology, (1978) 14/6 (659-672).  
 CODEN: BEPRDY  
 COUNTRY: France  
 DOCUMENT TYPE: Journal  
 FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery  
 026 Immunology, Serology and Transplantation  
 025 Hematology  
 006 Internal Medicine  
 LANGUAGE: French  
 SUMMARY LANGUAGE: English

AB To explain the frequency of post-surgical infections after cardiac surgery under extracorporeal circulation, the possible post-surgical decrease in immunoglobulin serum concentrations, the complement system and the

granulocyte functions were **measured** in 13 **cardiac** patients. The **measurements** for each patient were taken prior to the operation, and on the first and 8th days afterwards. Before surgery all the parameters were normal. On the first day after the operation the authors observed: (1) a moderate but statistically significant decrease in immunoglobulins (IgG, IgA and IgM) together with a decrease in the total hemolytic **complement** and its fractions (**C3**, C4 and C3 proactivator); (2) a significant decrease in the iodination and myeloperoxidase activity of the granulocyte; (3) an increase in the speed of granulocyte ingestion of microbes when the percentage of granulocytes which ensure this function is decreased; (4) On the 8th day after surgery, the serum components for immunity are normal; some of them (IgM, total hemolytic **complement**, **C3** and C3 proactivator) are increased. On the whole the functional activities of granulocytes are normal. These results suggest that the observed deficits on the 1st day after surgery facilitate the occurrence of infections.

L35 ANSWER 86 OF 87 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 76137487 EMBASE

DOCUMENT NUMBER: 1976137487

TITLE: Consumption of classical complement components by heart subcellular membranes in vitro and in patients after acute myocardial infarction.

AUTHOR: Neal Pinckard R.; Olson M.S.; Giclas P.C.; et al.

CORPORATE SOURCE: Dept. Microbiol., Univ. Arizona Coll. Med., Tucson, Ariz. 85724, United States

SOURCE: Journal of Clinical Investigation, (1975) 56/3 (740-750).  
CODEN: JCINAO

DOCUMENT TYPE: Journal

FILE SEGMENT: 026 Immunology, Serology and Transplantation  
006 Internal Medicine  
025 Hematology  
018 Cardiovascular Diseases and Cardiovascular Surgery

LANGUAGE: English

AB Experiments were conducted to characterize the antibody independent activation of complement in human serum by isolated human heart mitochondrial membranes in vitro and to determine whether similar patterns of complement consumption occurred in patients after acute myocardial infarction. Direct evidence for the interaction of C1 and heart mitochondrial membranes was obtained by mitochondria C1 binding and elution experiments. Exposure of normal human sera to isolated human heart mitochondria at 37.degree.C resulted in the consumption of C1, C4, C2, and C3 without significant consumption of the terminal components of the complement system (C6 through C9). The consumption occurred in the absence of **detectable** anti **heart** mitochondria autoantibody, was demonstrated to be calcium dependent, and was inhibited by either 0.01M EDTA or ethylene glycol bis(.beta. aminoethyl ether) N,N,N',N' tetraacetic acid (EGTA). Although specific absorption of Clq from human sera inhibited the mitochondria dependent activation of C4, C3 consumption was not affected. These data indicate that the consumption of C4 and C2 likely occurred due to the mitochondrial membrane mediated activation of C1, but that the consumption of the C3 did not necessarily involve either the classical or alternative complement pathways. After the in vitro characterization of the mitochondria dependent activation of the complement system, additional studies were performed to determine whether similar consumption occurred in patients after acute myocardial infarction. During a 72 h period after hospital admission significant decreases in C1, C4, and C3 occurred in six patients after acute myocardial infarction but not in six patients with recent chest pain but

no evidence of acute infarction. These studies suggest that myocardial cell necrosis results in the release of subcellular membrane constituents capable of activating the complement system in the absence of **detectable** anti **heart** autoantibodies; such activation may be responsible in part for the development of acute inflammation and evolution of the infarct size following coronary artery occlusion.

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ACCESSION NUMBER: 74083583 EMBASE

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TITLE: [Concentrations of sodium capobenate in the heart and blood after continuous intravenous infusion in the anesthetized rat].

TASSI EMATICI E CONCENTRAZIONI NEL MIOCARDIO DEL 3,4,5 TRIMETOSSIBENZOIL .epsilon. AMINOCAPROATO SODICO (C3) SOMMINISTRATO AL RATTO MEDIANTE INFUSIONE VENOSA CONTINUA.

AUTHOR: Baggio G.; Bernardi M.; Ferrari F.; et al.

CORPORATE SOURCE: Ist. Farmacol., Univ. Modena, Italy

SOURCE: Rivista di Farmacologia e Terapia, (1973) 4/2 (245-249).

CODEN: RVFTBB

DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index

030 Pharmacology

005 General Pathology and Pathological Anatomy

018 Cardiovascular Diseases and Cardiovascular Surgery

LANGUAGE: Italian

AB Rats were infused i.v. with sodium capobenate at 7.5 to 15 or 30 mg/kg/min. At different times during and after the infusion, blood radioactivity was **measured** and drug concentration calculated. Blood capobenate content increased as the quantity infused increased. Capobenate levels in blood declined very slowly after the infusion was stopped. The capobenate content of **heart** and blood was **measured** after i.v. infusion (7.5 to 15 and 30 mg/kg/min) for 30 min. Capobenate concentration was less in heart than in blood, but the ratio of concentrations in heart and blood differed with the dose injected.